

# STN SEARCH TRANSCRIPT

10/648,636 ~~10/936,18~~

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NEWS 27 AUG 11 Derwent World Patents Index(R) web-based training during  
August  
NEWS 28 AUG 11 STN AnaVist workshops to be held in North America  
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MACINTOSH VERSION IS V6.0c(ENG) AND V6.0c(JP),  
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005  
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ENTRY SESSION  
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STRUCTURE FILE UPDATES: 16 AUG 2005 HIGHEST RN 860495-66-5  
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\*\*\*\*\*  
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\* the IDE default display format and the ED field has been added. \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
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\*\*\*\*\*

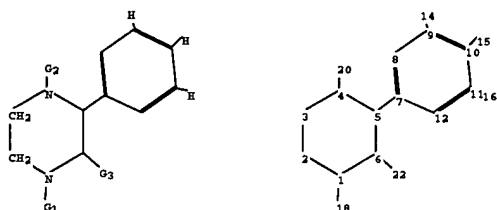
Structure search iteration limits have been increased. See HELP SLIMITS  
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Experimental and calculated property data are now available. For more  
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=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=>  
Uploading C:\Program Files\Stnexp\Queries\MIRTAZEPINE INTERMEDIATE.str



chain nodes :  
14 15 16 18 20 22  
ring nodes :  
1 2 3 4 5 6 7 8 9 10 11 12  
chain bonds :  
1-18 4-20 5-7 6-22 9-14 10-15 11-16  
ring bonds :  
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12  
exact/norm bonds :  
1-2 1-6 1-18 2-3 3-4 4-5 4-20 5-6 6-22  
exact bonds :  
5-7 9-14 10-15 11-16  
normalized bonds :  
7-8 7-12 8-9 9-10 10-11 11-12  
isolated ring systems :  
containing 1 : 7 :

G1:H,CH3

G2:H,CH2

G3:H,O

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 14:CLASS 15:CLASS 16:CLASS 18:CLASS 20:CLASS 22:CLASS

L1 STRUCTURE UPLOADED

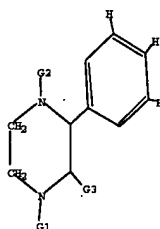
=> que L1

L2 QUE L1

=> D L2

L2 HAS NO ANSWERS

L1 STR



G1 H,Me

G2 H,CH2

G3 H,O

Structure attributes must be viewed using STN Express query preparation.  
L2 QUE ABB=ON PLU=ON L1

=> S L2 SSS FULL  
FULL SEARCH INITIATED 09:09:34 FILE 'REGISTRY'  
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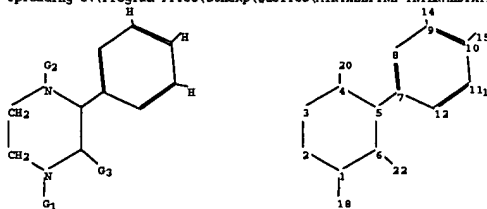
100.0% PROCESSED 129579 ITERATIONS 185 ANSWERS  
SEARCH TIME: 00.00.02

L3 185 SEA SSS FUL L1

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ENTER SCREEN EXPRESSION OR (END):end

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Uploading C:\Program Files\Stnexp\Queries\MIRTAZEPINE INTERMEDIATE.str



chain nodes :  
14 15 16 18 20 22

ring nodes :  
 1 2 3 4 5 6 7 8 9 10 11 12  
 chain bonds :  
 1-18 4-20 5-7 6-22 9-14 10-15 11-16  
 ring bonds :  
 1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12  
 exact/norm bonds :  
 1-2 1-6 1-18 2-3 3-4 4-5 4-20 5-6 6-22  
 exact bonds :  
 5-7 9-14 10-15 11-16  
 normalised bonds :  
 7-8 7-12 8-9 9-10 10-11 11-12  
 isolated ring systems :  
 containing 1 : 7 :

G1:H,CH3  
 G2:H,CH2  
 G3:H,O

Match level :  
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
 11:Atom 12:Atom 14:CLASS 15:CLASS 16:CLASS 18:CLASS 20:CLASS 22:CLASS

#### L4 STRUCTURE UPLOADED

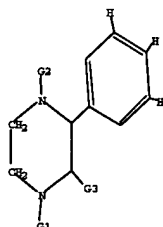
=> que L4

L5 QUE L4

=> D L5

L5 HAS NO ANSWERS

L4 STR



G1 H,Me

G2 H,CH2

G3 H,O

Structure attributes must be viewed using STN Express query preparation.

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CU, CZ, DE, DK, DM, DO, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GN, GU, HD, IL, IN, IS, JP, KE, KG, KH, KI, KM, KN, LA, LB, LC, LR, LS, LT, LU, LV, MA, MD, ME, MG, MH, MI, MN, MO, MP, MQ, MR, MS, MT, MU, NA, NC, NE, NG, NI, NL, NO, NZ, OM, OS, PA, PE, PG, PH, PK, PL, PT, PU, PY, RA, RB, RE, RF, RH, RI, RJ, RK, RL, RM, RO, RS, RU, RW, SA, SB, SC, SD, SE, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SR, SS, ST, SU, SV, SW, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TR, TT, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UR, US, UT, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ.

PRIORITY APPLN. INFO.:  
 US 2003-531927P P 20031222  
 US 2004-548090P P 20040224  
 US 2004-548040P P 20040227

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to a group of novel amino-substituted dibenzazepines I, benzazepines II and related clozapine analogs, which are agonists of muscarinic receptors. In compds. I and II, W is N, CH, O, or S; Y is N, O, or CH; R1, R6, and R7 are independently absent or selected from H, halo, amino, (un)substituted C1-20 alkyl, (un)substituted C3-8 cycloalkyl, (un)substituted aryl, etc., or R1R6 is -CH2CH2-; each R2, R3, R4, and R5 is independently selected from H, halo, (un)substituted C1-6 alkyl, (un)substituted C1-6 alkoxy, cyano, etc., or R2 and R3, or R3 and R4, or R4 and R5 taken together, along with the ring carbons to which they are attached, form a 5- or 6-membered cycloalkyl, heterocyclyl or heteroaryl ring, or a 6-membered aryl ring; Z is (un)substituted NH, O, S, or CH2; and R8 and R9 are independently selected from H, halo, (un)substituted C1-6 alkyl, (un)substituted C1-6 alkoxy, cyano, etc., or R8 and R9 taken together, along with the ring carbons to which they are attached, form a 5- or 6-membered cycloalkyl, heterocyclyl or heteroaryl ring, or a 6-membered aryl ring; including pharmaceutically acceptable salts, esters, amides or prodrugs of these, provided that compound I is not clozapine or N-desmethyloclozapine. The invention also relates to the preparation of I, preparation of a combinatorial library of compds. I, pharmaceutical compds. containing compound I with a physiol. acceptable carrier, diluent, or excipient.

optionally including a neuropsychiatric agent as well as to the use of the compds. for treating neuropsychiatric disorders. Substitution of 4-chloro-2-fluorobenzene with 2-amino-5-chlorobenzoic acid followed by reduction of the nitro group, ring-closing coupling, and condensation with piperazine gave dibenzodiazepine III. The compds. of the invention express efficacy (eff) at muscarinic M1 receptors in the range of -11 to 92 and potency (expressed as pEC50) of 5.5 to 7.2; the compds. had eff at M2 receptors of -14 to 187 and pEC50 of 5.4 to 6.6.

IT 5271-26-1, 2-Phenylpiperazine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (starting material; preparation of amino-substituted diarylcycloheptene analogs as muscarinic agonists and methods of treatment of neuropsychiatric disorders)

RN 5271-26-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L5 QUE ABB-ON FLU-ON L4

=> S L5 SSS FULL  
 FULL SEARCH INITIATED 09:10:42 FILE 'REGISTRY'  
 FULL SCREEN SEARCH COMPLETED - 129579 TO ITERATE

100.0% PROCESSED 129579 ITERATIONS 181 ANSWERS  
 SEARCH TIME: 00.00.04

L6 181 SEA SSS FUL L4

=> FILE CAPLUS  
 COST IN U.S. DOLLARS  
 FULL ESTIMATED COST 326.53 326.74

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 FILE LAST UPDATED: 16 Aug 2005 (20050816/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L6

L7 120 L6

=> D 1-120 IBIB ABS HITSTR

L7 ANSWER 1 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 2005:612094 CAPLUS  
 DOCUMENT NUMBER: 143:133403  
 TITLE: Amino-substituted diaryl[a,d]cycloheptene analogs as muscarinic agonists, their preparation and use in the treatment of neuropsychiatric disorders  
 INVENTOR(S): Ek, Fredrik; Olsson, Roger; Ohlsson, Joergen  
 PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA  
 SOURCE: PCT Int. Appl., 129 pp.  
 CODEN: PIKX02  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005063254	A2	20050714	WO 2004-US43224	20041221

L7 ANSWER 2 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 2005:23845 CAPLUS  
 DOCUMENT NUMBER: 143:47878  
 TITLE: Synthesis of 2-phenylpiperazine  
 AUTHOR(S): Xu, Yungen; Han, Chunxia; Gu, Jinfeng; Luo, Sui  
 CORPORATE SOURCE: Center of Drug Discovery, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China  
 SOURCE: Zhongguo Yiyao Gongye Zazhi (2003), 34(11), 545-546  
 CODEN: ZYGGZ; ISSN: 1001-8255  
 PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese  
 OTHER SOURCE(S): CASREACT 143:47878  
 AB 2-Phenylpiperazine, an intermediate of mirtazapine was synthesized from phenylacetic acid by reaction with phosphorus trichloride and bromine to give Et a-bromophenyl acetate which reacted with ethylenediamine followed by reduction with lithium aluminum hydride. The overall yield was 31.7%.  
 IT 5271-26-16, 2-Phenylpiperazine 5368-28-5P  
 EL: SYN (Synthetic preparation); PREP (Preparation) (synthesis of 2-phenylpiperazine)  
 RN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 5368-28-5 CAPLUS  
 CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 3 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 2004:1036760 CAPLUS  
 DOCUMENT NUMBER: 143:23309  
 TITLE: Process for preparing 1-methyl-3-phenylpiperazine using a novel intermediate  
 INVENTOR(S): Handa, Vijay Kumar; Rao, Divvula Venkata Naga Srinivasa; Sivakumaran, Memakshisunderan  
 PATENT ASSIGNEE(S): India  
 SOURCE: U.S. Pat. Appl. Publ., 6 pp.  
 CODEN: USMXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

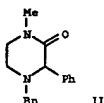
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004242979	A1	20041202	US 2003-548636	20030826
WO 2004106309	A1	20041209	WO 2004-1B1125	20040329

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

\* APPLICANTS \*

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MH, MI, MK, MN, MO, NP, NR, NU, NZ, OM, PA, PE, PG, PH, PL, PT, PU, PY, RE, RO, RU, SC, SD, SE, SG, SH, SI, SJ, SK, SL, SM, SN, SV, SW, SY, SZ, TD, TH, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VE, VU, ZA, ZM, ZW, ZY, AA, AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK, AL, AM, AN, AO, AP, AQ, AR, AS, AT, AU, AV, AW, AX, AY, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TT, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UU, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ.

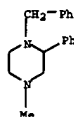
PRIORITY APPL. INFO.: IN 2003-MA442 A 20030602  
OTHER SOURCE(S): CASREACT 142:23309  
GI



AB The present invention describes an industrially advantageous process to prepare highly pure 1-methyl-3-phenylpiperazine (I) that makes use of a novel piperazine derivative, 4-benzyl-1-methyl-2-oxo-3-phenylpiperazine (II). The compound I is a useful intermediate in the preparation of antidepressant Mirtazapine. Thus, 100 g 4-benzyl-1-methyl-2-oxo-3-phenylpiperazine was added dropwise over 30 min to a suspension of 15.3 g NaH (65% dispersion in oil) in DMF, followed by slowly adding 44 g MeI in 50 mL DMF in 45° at <25°, and the mixture was allowed to react for 1 h to give, after workup and crystallization from cyclohexane, 98.5 g I (93.8%). II (90 g) was added slowly in 1 h at 10-15° to a suspension of LiAlH<sub>4</sub> in 450 mL THF and then the reaction mixture was refluxed for 6 h, quenched by successively adding 45 mL H<sub>2</sub>O and 15% aqueous NaOH, and stirred at 20-25° for 1 h to give, after workup, 80 g 4-benzyl-1-methyl-3-phenylpiperazine (III) (80%). III (40 g) was dissolved in 300 mL AcOH, treated with 3 g 5% Pd-C, and hydrogenated at 80-100 psi and 25-30° for 4 h to give, after workup, I (100% HPLC purity).

IT 23174-98-3P, 4-Benzyl-1-methyl-3-phenylpiperazine  
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
[intermediate; process for preparing high-purity 1-methyl-3-phenylpiperazine using 4-benzyl-1-methyl-2-oxo-3-phenylpiperazine as novel intermediate]

RN 23174-98-3 CAPLUS  
CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT 5271-27-2P, 1-Methyl-3-phenylpiperazine  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

AB 2-(Methylsulfonyl)-2-(p-tolylsulfonyl)oxiranes were easily prepared by the condensation of methylthiomethyl p-tolyl sulfone with aldehydes and the subsequent oxidation with MCPBA. They smoothly reacted with primary or secondary amines to give α-amino carboxamides, e.g., I, in high yield. This reaction was extended to the reaction with diaminoalkanes to form the corresponding 2,5-disubstituted oxiranes, 2,4-disubstituted oxiranes, or 2,7-disubstituted oxiranes. The reaction of the oxiranes with some related compounds, having two nucleophilic sites are also described.

IT 5368-28-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
[preparation of α-amino carboxamides via condensation of methylthiomethyl tolyl sulfone with aldehydes followed by epoxidation, ring opening/oxidation with amines and diamines]

RN 5368-28-5 CAPLUS  
CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:606436 CAPLUS  
DOCUMENT NUMBER: 141:157135  
TITLE: Preparation of piperidine and piperazine derivatives with dopaminergic neurotransmitter system activity for diagnostic and therapeutic uses  
INVENTOR(S): Elmaleh, David R.; Choi, Sangwoon; Fishman, Alan J.  
PATENT ASSIGNEE(S): The General Hospital Corporation, USA  
SOURCE: PCT Int. Appl., 49 pp.  
CODEN: PIKXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063150	A2	20040728	WO 2003-US41731	20031231
WO 2004063150	A3	20050602		

W: AK, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BE, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MH, MI, MK, MN, MO, NP, NR, NU, NZ, OM, PG, PH, PL, PT, PU, PY, RE, RO, RU, SC, SD, SE, SG, SH, SI, SJ, SK, SL, SM, SN, SV, SW, SY, SZ, TD, TH, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VE, VU, ZA, ZM, ZW, ZY, AA, AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK, AL, AM, AN, AO, AP, AQ, AR, AS, AT, AU, AV, AW, AX, AY, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TT, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UU, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ.

PRIORITY APPL. INFO.: MARPAT 141:157135  
OTHER SOURCE(S):  
GI

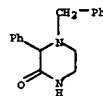
(Preparation)  
[process for preparing high-purity 1-methyl-3-phenylpiperazine using 4-benzyl-1-methyl-2-oxo-3-phenylpiperazine as novel intermediate]

RN 5271-27-2 CAPLUS  
CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

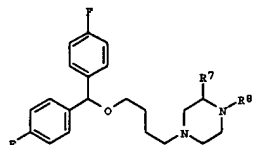
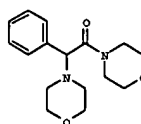


IT 5368-23-0, 4-Benzyl-2-oxo-3-phenylpiperazine  
RL: RCT (Reactant); RACT (Reactant or reagent)  
[reactant; process for preparing high-purity 1-methyl-3-phenylpiperazine using 4-benzyl-1-methyl-2-oxo-3-phenylpiperazine as novel intermediate]

RN 5368-23-0 CAPLUS  
CN Piperazine, 3-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



L7 ANSWER 4 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:887366 CAPLUS  
DOCUMENT NUMBER: 142:56271  
TITLE: Novel synthesis of α-amino carboxamides and their related compounds via α-oxo sulfones starting from 2,2-disulfonyloxiranes  
AUTHOR(S): Matsumoto, Shoji; Ishii, Michiko; Kimura, Kazuo; Ogura, Katsuyuki  
CORPORATE SOURCE: Department of Applied Chemistry and Biotechnology, Faculty of Engineering, Chiba University, Chiba, 263-8522, Japan  
SOURCE: Bulletin of the Chemical Society of Japan (2004), 77(10), 1897-1903  
CODEN: BCSJAB; ISSN: 0009-2673  
PUBLISHER: Chemical Society of Japan  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB Piperazine derivs., such as I [R<sup>7</sup> = H, Ph, O; R<sup>8</sup> = H, Ph, COMe, COPh, halophenyl, nitrophenyl, nitrophenylsulfonyl, piperonyl], were prepared for use in treating neurodegenerative diseases characterized by the lack of dopamine neurons activity or for imaging the dopamine neurons. Thus, piperazine derivative II (R<sup>7</sup> = R<sup>8</sup> = H) was prepared via an amination reaction with 30% yield of (P-4-C6H4)2CHO(CH<sub>2</sub>)4Cl and piperazine using K<sub>2</sub>CO<sub>3</sub> in DMF. The prepared piperazines were assayed for binding affinities at the DA, 5-HT and NE transporters labeled with [125I]RTI-55.

IT 5271-26-1P, 2-Phenylpiperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
[preparation of piperidine and piperazine derivs. with dopaminergic neurotransmitter system activity for diagnostic and therapeutic uses]

RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 5368-28-5 CAPLUS  
CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)

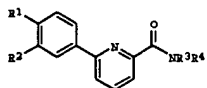


L7 ANSWER 6 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:586832 CAPLUS  
DOCUMENT NUMBER: 141:140318  
TITLE: Preparation of (phenyl)pyridine derivatives as selective phosphodiesterase 4 inhibitors for treatment of respiratory disorders  
INVENTOR(S): Iwata, Masahiro; Kono, Norimasa; Katsawa, Hiroyuki; Takawa, Tomofumi; Tsukamoto, Kazumari; Seo, Tatsushi; Yahiyo, Kiyoshi; Kobayashi, Tsuyoshi; Takeuchi, Makoto; Yoshida, Shinya; Nakamura, Haruka  
PATENT ASSIGNEE(S): Yamamoto Pharmaceutical Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 58 pp.  
CODEN: JKKXAF  
DOCUMENT TYPE: Patent

LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004203871	A2	20040722	JP 2003-414006	20031212
PRIORITY APPL. INFO.:			JP 2003-361550	A 20021213
OTHER SOURCE(S):			CASREACT 141:140310; MARPAT 141:140310	

GI



AB Title compns., useful for treatment of asthma and chronic obstructive pulmonary disease, contain pyridines I (R1, R2 = H, halo, lower alkyl, (oxy), (lower alkyl)amino, O-lower alkylene-NH-lower alkyl, hetero-lower alkylene, etc.), R1R2 may be linked to form lower alkylene, R3 = lower alkyl, lower alkynyl, (un)substituted cyclic hydrocarbyl, (un)substituted heterocyclic, etc., R4 = H, lower alkyl, lower alkynyl, lower alkynyl, (un)substituted cyclic hydrocarbyl, (un)substituted heterocyclic, etc.) or their pharmaceutically acceptable salts, and carriers. Thus, amidation of 6-[3,4-dimethoxyphenyl]pyridine-2-carboxylic acid with 4-(4-methoxyphenyl)piperazine gave I (R1 = R2 = MeO, R3R4 = 4-(4-methoxyphenyl)piperazinyl), which inhibited phosphodiesterase 4 with IC50 of <12 nM.

IT 5368-28-5, 2-Oxo-3-phenylpiperazine  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of pyridines as selective phosphodiesterase 4 inhibitors for treatment of respiratory disorders)

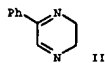
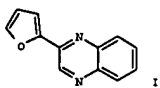
RN 5368-28-5 CAPLUS

CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:410230 CAPLUS  
DOCUMENT NUMBER: 140:375104  
TITLE: An improved process for the preparation of  $\alpha$ -substituted piperazines  
INVENTOR(S): Sengupta, Sreela; Sahu, Devi Prasad; Chatterjee, Sunil Krishna  
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India  
SOURCE: Indian, 12 pp.  
CODEN: INXXAP  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

GI



AB  $\alpha$ -Hydroxy ketones underwent manganese dioxide-mediated oxidation followed by trapping with aromatic or aliphatic 1,2-diamines to give quinoxalines, e.g., I, or dihydropyrazines, e.g., II, resp., in a one-pot procedure, avoiding the need to isolate the highly reactive dicarbonyl intermediates. The scope, limitations, and modifications of this procedure, in which reduction was carried out in the same reaction vessel, generating piperazines, or oxidation, leading to pyrazines, are also discussed.

IT 5271-26-18, 2-Phenylpiperazine  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of piperazines via oxidation of  $\alpha$ -hydroxy ketones followed by reductive heterocyclization with aliphatic diamines)

RN 5271-26-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

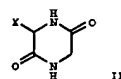
L7 ANSWER 9 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:696533 CAPLUS  
DOCUMENT NUMBER: 139:230789  
TITLE: Preparation of 2-phenylpiperazine derivatives as tachykinin antagonists  
INVENTOR(S): Ogino, Takeshi; Komishi, Yukari; Higashitara, Kunihiko; Furukawa, Kazuhito  
PATENT ASSIGNEE(S): Nippon Zoki Pharmaceutical Co., Ltd., Japan  
SOURCE: U.S. Pat. Appl. Publ., 18 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003166616	A1	20030904	US 2003-370918	20030220
US 6906074	B2	20050614		
CA 2419665	AA	20030822	CA 2003-2419665	20030221
JP 2003313173	A2	20031106	JP 2003-43980	20030221
PRIORITY APPL. INFO.:			JP 2002-45562	A 20020222
OTHER SOURCE(S):			MARPAT 139:230789	

GI

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 179274	A	19970920	IN 1992-DE1075	19921120
PRIORITY APPL. INFO.:			IN 1992-DE1075	19921120
OTHER SOURCE(S):			CASREACT 140:375104	

GI



AB An improved process for the preparation of  $\alpha$ -substituted piperazines [I; X = Ph, indolylmethyl] which comprises adding dropwise BF<sub>3</sub>·Et<sub>2</sub>O to 2,5-diketopiperazine II [X has the meaning given above] and an excess of NaBH<sub>4</sub> in an aprotic solvent to form BZH<sub>6</sub> in situ, heating the resulting mixture at a temperature in the range of 5-65°C for 8-36 h to complete the reaction to yield  $\alpha$ -substituted piperazine I [X has the meaning given above]. Thus, adding BF<sub>3</sub>·Et<sub>2</sub>O to a solution of (R)-3-phenyl-2,5-diketopiperazine and NaBH<sub>4</sub> in THF followed by refluxing for 12 h afforded 91% (R)-(-)-2-phenylpiperazine.HCl.

IT 584283-07-6P  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(improved process for the preparation of  $\alpha$ -substituted piperazines)

RN 584283-07-6 CAPLUS

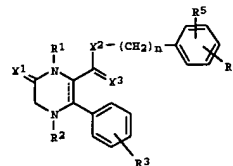
CN Piperazine, 2-phenyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

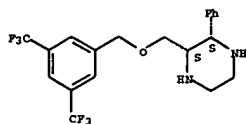
Absolute stereochemistry. Rotation (-).



•x HCl

L7 ANSWER 8 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:154043 CAPLUS  
DOCUMENT NUMBER: 140:423642  
TITLE: Tandem oxidation processes for the preparation of nitrogen-containing heteroaromatic and heterocyclic compounds  
AUTHOR(S): Raw, Steven A.; Wilfred, Cecilia D.; Taylor, Richard J. K.  
CORPORATE SOURCE: Department of Chemistry, University of York, Heslington, YO10 5DD, UK  
SOURCE: Organic & Biomolecular Chemistry (2004), 2(5), 788-796  
CODEN: OBCHAK; ISSN: 1477-0520  
PUBLISHER: Royal Society of Chemistry  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 140:423642

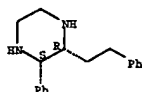




● 2 HCl

RN 586396-80-7 CAPLUS  
CN Piperazine, 2-phenyl-3-(2-phenylethyl)-, dihydrochloride, (2S,3R)- (9CI)  
(CA INDEX NAME)

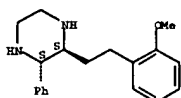
Absolute stereochemistry.



● 2 HCl

RN 586396-81-8 CAPLUS  
CN Piperazine, 2-(2-(2-methoxyphenyl)ethyl)-3-phenyl-, dihydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

RN 586397-03-7 CAPLUS  
CN Piperazine, 3-[[[3,5-bis(trifluoromethyl)phenyl]methoxy]methyl]-2-phenyl-1-(phenylmethyl)-, dihydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RL: SPN (Synthetic preparation); PREP (Preparation)  
(Preparation of quinoxalines, dihydropyrazines, pyrazines, and piperazines via MnO<sub>2</sub>-mediated oxidation of α-hydroxy ketones and subsequent trapping with aromatic or aliphatic 1,2-diamines)

RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:675554 CAPLUS  
DOCUMENT NUMBER: 139:197510  
TITLE: Preparation of 2-phenylpiperazine derivatives as tachykinin antagonists  
INVENTOR(S): Ogino, Takashi; Konishi, Yukari; Higashihara, Kunihiro; Furukawa, Kazuhito  
PATENT ASSIGNEE(S): Nippon Zoki Pharmaceutical Co., Ltd., Japan  
SOURCE: Eur. Pat. Appl., 25 pp.  
CODEN: EPXNDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

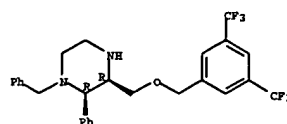
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1330592	A1	20030827	EP 2003-3241	20030221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPL. INFO.: EP 2003-3241 20030221				
OTHER SOURCE(S): MARPAT 139:197510				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB 2-Phenylpiperazines I [X1, Y3 = O, R2, X2 = O, NH, NMe; n = 0, 1; R1 = H, alkyl; R3 = H, CH, tetrazolyl, aminotriazolyl, mesyl, CO<sub>2</sub>OMe], (un)substituted alkyl; R4 = H, halogen, alkyl, alkoxy; R5 = H, alkoxy, CF<sub>3</sub>] were prepared for use as tachykinin antagonists. Thus, the piperazine II was prepared from D-serine and has IC<sub>50</sub> for human NK1 receptor binding of 0.04 nMol/L and had a much stronger inhibitory effect against tachykinin-induced increase in vascular permeability than LY-303870.

IT 586396-79-4P 586396-80-7F 586396-81-8P  
586397-03-7P 586397-07-1P  
RL: SPN (Synthetic preparation); TRU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(Preparation of 2-phenylpiperazine derivate as tachykinin antagonists)  
RN 586396-79-4 CAPLUS  
CN Piperazine, 2-[[[3,5-bis(trifluoromethyl)phenyl]methoxy]methyl]-3-phenyl-, dihydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

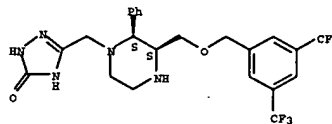
Absolute stereochemistry.



● 2 HCl

RN 586397-07-1 CAPLUS  
CN 3H-1,2,4-Triazol-3-one, 5-[[[(2S,3S)-3-[[[3,5-bis(trifluoromethyl)phenyl]methoxy]methyl]-2-phenyl-1-piperazinyl]methyl]-1,2-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)

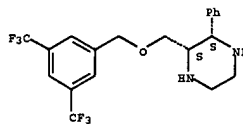
Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

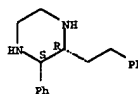
L7 ANSWER 10 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:687441 CAPLUS  
DOCUMENT NUMBER: 140:27801  
TITLE: Preparation of quinoxalines, dihydropyrazines, pyrazines, and piperazines using tandem oxidation processes  
AUTHOR(S): Raw, Steven A.; Wilfred, Cecilia D.; Taylor, Richard J. R.  
CORPORATE SOURCE: Department of Chemistry, University of York, York, YO10 5DD, UK  
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2003), (18), 2286-2287  
CODEN: CHCOPL, ISSN: 1359-7345  
PUBLISHER: Royal Society of Chemistry  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 140:27801  
AB α-Hydroxy ketones undergo MnO<sub>2</sub>-mediated oxidation followed by in situ trapping with aromatic or aliphatic 1,2-diamines to give quinoxalines or dihydropyrazines, resp., in a one pot procedure which avoids the need to isolate the highly reactive 1,2-dicarbonyl intermediates. Modifications of the procedure allow the formation of pyrazines and piperazines.  
IT 5271-26-1P



● 2 HCl

RN 586396-80-7 CAPLUS  
CN Piperazine, 2-phenyl-3-(2-phenylethyl)-, dihydrochloride, (2S,3R)- (9CI)  
(CA INDEX NAME)

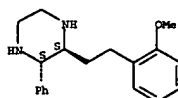
Absolute stereochemistry.



● 2 HCl

RN 586396-81-8 CAPLUS  
CN Piperazine, 2-(2-(2-methoxyphenyl)ethyl)-3-phenyl-, dihydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

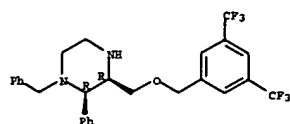
Absolute stereochemistry.



● 2 HCl

RN 586397-03-7 CAPLUS  
CN Piperazine, 3-[[[3,5-bis(trifluoromethyl)phenyl]methoxy]methyl]-2-phenyl-1-(phenylmethyl)-, dihydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

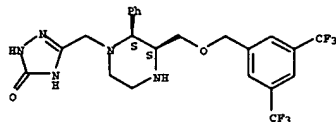
Absolute stereochemistry.



● 2 HCl

EN 586397-07-1 CAPLUS  
CN 3E-1,2,4-Triazol-3-one, 5-[[[(2S,3S)-3-[[[3,5-bis(trifluoromethyl)phenyl]methoxy)methyl]-2-phenyl-1-piperazinyl]methyl]-1,2-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:434554 CAPLUS  
DOCUMENT NUMBER: 139:22224  
TITLE: Preparation of pyridine and pyrimidine derivatives as p38 kinase inhibitors  
INVENTOR(S): Davis, Jeremy Martin; Langham, Barry John; Naik, Manisha; Brookings, Daniel Christopher; Cubben, Rachel Jane; Franklin, Richard Jeremy  
PATENT ASSIGNEE(S): Celltech R & D Limited, UK  
SOURCE: PCT Int. Appl., 104 pp.  
CODEN: PIKXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

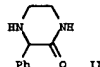
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045941	A1	20030605	WO 2002-GB5196	20021120

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH,



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:395665 CAPLUS  
DOCUMENT NUMBER: 139:180038  
TITLE: An efficient process for preparing 1-methyl-3-phenylpiperazine hydrochloride and its derivatives  
AUTHOR(S): Guo, Bai Shu; Yang, Yu She; Ji, Ru Yun  
CORPORATE SOURCE: Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, P. R. China  
SOURCE: Chinese Chemical Letters (2003), 14(4), 365-367  
CODEN: CCLEET; ISSN: 1001-8417  
PUBLISHER: Chinese Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 139:180038  
GI



AB An improved method for preparation of the title compound (I-HCl) from 3-phenyl-2-piperazine (II) via benzylation at N-4, reduction of the CO group, methylation at N-1, and deprotection of N-4 was described. The overall yield of I-HCl from II was ~80%.

IT 5368-28-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 1-methyl-3-phenylpiperazine hydrochloride)

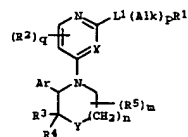
EN 5368-28-5 CAPLUS  
CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



IT 5368-23-0F 577955-33-0F  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 1-methyl-3-phenylpiperazine hydrochloride)

EN 5368-23-0 CAPLUS  
CN Piperazinone, 3-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: GE, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GF, GQ, GW, ML, MR, NE, SN, TD, TG  
EP 1448555 A1 20040825 EP 2002-777562 20021120  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
US 2005080258 A1 20050414 US 2003-495885 20021120  
PRIORITY APPL. INFO.: GB 2001-27929 A 20011121  
WO 2002-GB5196 W 20021120  
OTHER SOURCE(S): MARPAT 139:22224  
GI



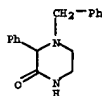
AB Title compds. I (X = N, (un)substituted CH; Y = O, S, S(O), SO<sub>2</sub>, (un)substituted CH<sub>2</sub>, NH; when R<sub>3</sub>R<sub>4</sub> = O, S, Y = (un)substituted CH<sub>2</sub>, NH; L<sub>1</sub> = covalent bond, linker atom or group; Alk = (un)substituted aliphatic, heteroaliph.; p = 0, 1; n = 0-3; when n = 0, Y = (un)substituted CH<sub>2</sub>; Ar = (un)substituted aromatic, heteroarom.; m = 0-3; q = 0-2; R<sub>1</sub> = H, halogen, CN, NO<sub>2</sub>, (un)substituted cycloaliph., polycycloaliph., heterocycloaliph., aromatic, heteroarom.; when L<sub>1</sub> = bond and p = 0, R<sub>1</sub> = H, halogen, CN, NO<sub>2</sub>; R<sub>2</sub> = H, halogen, CN, (un)substituted alkyl, CH, SH, CO<sub>2</sub>H; R<sub>3</sub>, R<sub>4</sub> = H, R<sub>5</sub>; R<sub>3</sub>R<sub>4</sub> = O, S; R<sub>5</sub> = H, O, S, (un)substituted alkyl, CH, SH, CN, CO<sub>2</sub>H) were prepared for use as p38 kinase inhibitors, useful in the treatment of immune or inflammatory disorders. Thus, PhCH<sub>2</sub>CO<sub>2</sub>Me was cyclized with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> to give 3-phenyl-2-piperazine which was treated with 2,4-dichloropyrimidine and 3-F<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NH<sub>2</sub> to give 3-phenyl-4-[2-(3-trifluoromethylbenzylamino)pyrimidin-4-yl]piperazin-2-one.

IT 5271-26-1F, 2-Phenylpiperazine 5368-28-5F,  
3-Phenyl-2-piperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of pyridine and pyrimidine derivs. as p38 kinase inhibitors)

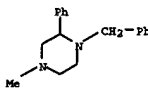
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



EN 5368-28-5 CAPLUS  
CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



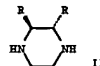
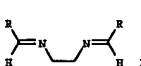
EN 577955-33-0 CAPLUS  
CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:275607 CAPLUS  
DOCUMENT NUMBER: 139:6841  
TITLE: Diastereoselective Synthesis of Piperazines by Manganese-Mediated Reductive Cyclization  
AUTHOR(S): Mercer, Gregory J.; Sigman, Matthew S.  
CORPORATE SOURCE: Department of Chemistry, University of Utah, Salt Lake City, UT, 84112-8500, USA  
SOURCE: Organic Letters (2003), 5(9), 1591-1594  
CODEN: ORLEP7; ISSN: 1522-7060  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 139:6841  
GI



AB Trans aryl-substituted piperazine were prepared via a simple and effective synthesis using a Bronsted acid and manganese(0). Thus, reaction of the bis(imines) I (R = Ph, 2,5-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, 2,4-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, 4-MeOC<sub>6</sub>H<sub>4</sub>, 4-ClC<sub>6</sub>H<sub>4</sub>, 2-furyl, 2-naphthyl) in MeCN/toluene containing pyridine hydrochloride or F<sub>3</sub>CCO<sub>2</sub>H and Mn(0) at room temperature for 8-24 h gave the piperazines II in 80-99% yields.

IT 81602-00-8F  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(diastereoselective preparation of diarylpiperazines by Mn mediated)

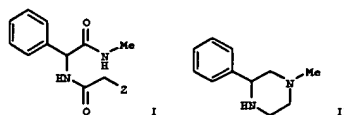
reductive cyclization of bis(imines))  
EN 81602-00-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)  
Relative stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STM  
ACCESSION NUMBER: 2003:242289 CAPLUS  
DOCUMENT NUMBER: 138:254962  
TITLE: Substituted phenylacetamide derivatives and phenylmethylpiperazine as intermediate compounds for the preparation of mirtazapine and the production methods thereof  
INVENTOR(S): Bosch i Llado, Jordi; Camps Garcia, Pelayo; Contreras Lascore, Juan; Onrubia Miguel, Maria del Carmen  
PATENT ASSIGNEE(S): Medichem S.A., Spain  
SOURCE: PCT Int. Appl., 19 pp.  
CODEN: PIKXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Spanish  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024918	A1	20030327	WO 2001-ES347	20010914
W: AB, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
HW: GM, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, CO, GW, ML, MR, NE, SN, TD, TG				
CA 2460571	AA	20030327	CA 2001-2460571	20010914
EP 1426356	A1	20040609	EP 2001-969812	20010914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004236107	A1	20041125	US 2004-488909	20040304
CO, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPL. INFO.: US 2001-25347 W 20010914				
OTHER SOURCE(S): CASREACT 138:254962; MARPAT 138:254962				
GI				



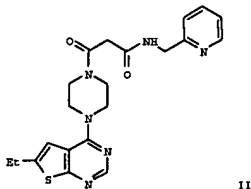
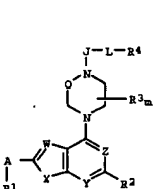
AB The invention relates to novel compds. I [Z = leaving group subject to nucleophilic displacement], which are intermediates used in the preparation of the antidepressant mirtazapine, and to production methods for them. The invention method is used to produce (2)-3-phenyl-1-methylpiperazine (II), which is also an important intermediate for the production of mirtazapine. The preparative method involves cyclization of I in the presence of a reducing agent. The invention also relates to a method of producing I. For instance, esterification of DL-  $\alpha$ -phenylglycine in MeOH in the presence of EtCl at room temperature gave 94.3% Me ester, which reacted with MeNH<sub>2</sub> in aqueous solution at 21° (slightly exothermic) to give 99.6% N-methylamide. Reaction of the latter with ClCH<sub>2</sub>COCl in acetone in the presence of Na<sub>2</sub>CO<sub>3</sub> at 0-5° gave 83.5% I [Z = Cl] with 99.9% purity. Reductive cyclization of this chloro diamide using BH<sub>3</sub>·THF in refluxing THF (81.9%) or NaBH<sub>4</sub> and HCl in MeOCH<sub>2</sub>CH<sub>2</sub>OMe at 0-5° (96.15%) gave I.  
IT 5271-27-2F, (2)-3-Phenyl-1-methylpiperazine  
RL: IMF (Industrial manufacture); SPW (Synthetic preparation); PREP (Preparation)  
(invention intermediate; preparation of (chloroacetamido)methylphenylacetamide and phenylmethylpiperazine as intermediates for mirtazapine)  
EN 5271-27-2 CAPLUS  
CN Piperazine, 1-methyl-3-phenyl-, (7CI, 8CI, 9CI) (CA INDEX NAME)



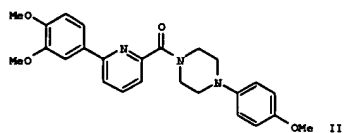
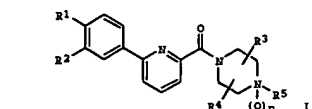
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STM  
ACCESSION NUMBER: 2003:221465 CAPLUS  
DOCUMENT NUMBER: 138:255249  
TITLE: Preparation of piperazine and homopiperazine compounds useful in the treatment of thrombosis and to inhibit ADP-mediated platelet aggregation  
INVENTOR(S): Levy, Daniel E.; Smyth, Mark S.; Scarborough, Robert M.  
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 260 pp.  
CODEN: PIKXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022214	A2	20030320	WO 2002-US28618	20020906
WO 2003022214	A3	20040325		
W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
HW: GM, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 200315556	A1	20030814	US 2002-237153	20020906
PRIORITY APPL. INFO.: US 2001-317192P P 20010906				
OTHER SOURCE(S): MARPAT 138:255249				
GI				



AB Piperazine and homopiperazine compds. I, wherein O is (CH<sub>2</sub>)<sub>n</sub>, n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000, 1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1020, 1021, 1022, 1023, 1024, 1025, 1026, 1027, 1028, 1029, 1030, 1031, 1032, 1033, 1034, 1035, 1036, 1037, 1038, 1039, 1040, 1041, 1042, 1043, 1044, 1045, 1046, 1047, 1048, 1049, 1050, 1051, 1052, 1053, 1054, 1055, 1056, 1057, 1058, 1059, 1060, 1061, 1062, 1063, 1064, 1065, 1066, 1067, 1068, 1069, 1070, 1071, 1072, 1073, 1074, 1075, 1076, 1077, 1078, 1079, 1080, 1081, 1082, 1083, 1084, 1085, 1086, 1087, 1088, 1089, 1090, 1091, 1092, 1093, 1094, 1095, 1096, 1097, 1098, 1099, 1100, 1101, 1102, 1103, 1104, 1105, 1106, 1107, 1108, 1109, 1110, 1111, 1112, 1113, 1114, 1115, 1116, 1117, 1118, 1119, 1120, 1121, 1122, 1123, 1124, 1125, 1126, 1127, 1128, 1129, 1130, 1131, 1132, 1133, 1134, 1135, 1136, 1137, 1138, 1139, 1140, 1141, 1142, 1143, 1144, 1145, 1146, 1147, 1148, 1149, 1150, 1151, 1152, 1153, 1154, 1155, 1156, 1157, 1158, 1159, 1160, 1161, 1162, 1163, 1164, 1165, 1166, 1167, 1168, 1169, 1170, 1171, 1172, 1173, 1174, 1175, 1176, 1177, 1178, 1179, 1180, 1181, 1182, 1183, 1184, 1185, 1186, 1187, 1188, 1189, 1190, 1191, 1192, 1193, 1194, 1195, 1196, 1197, 1198, 1199, 1200, 1201, 1202, 1203, 1204, 1205, 1206, 1207, 1208, 1209, 1210, 1211, 1212, 1213, 1214, 1215, 1216, 1217, 1218, 1219, 1220, 1221, 1222, 1223, 1224, 1225, 1226, 1227, 1228, 1229, 1230, 1231, 1232, 1233, 1234, 1235, 1236, 1237, 1238, 1239, 1240, 1241, 1242, 1243, 1244, 1245, 1246, 1247, 1248, 1249, 1250, 1251, 1252, 1253, 1254, 1255, 1256, 1257, 1258, 1259, 1260, 1261, 1262, 1263, 1264, 1265, 1266, 1267, 1268, 1269, 1270, 1271, 1272, 1273, 1274, 1275, 1276, 1277, 1278, 1279, 1280, 1281, 1282, 1283, 1284, 1285, 1286, 1287, 1288, 1289, 1290, 1291, 1292, 1293, 1294, 1295, 1296, 1297, 1298, 1299, 1300, 1301, 1302, 1303, 1304, 1305, 1306, 1307, 1308, 1309, 1310, 1311, 1312, 1313, 1314, 1315, 1316, 1317, 1318, 1319, 1320, 1321, 1322, 1323, 1324, 1325, 1326, 1327, 1328, 1329, 1330, 1331, 1332, 1333, 1334, 1335, 1336, 1337, 1338, 1339, 1340, 1341, 1342, 1343, 1344, 1345, 1346, 1347, 1348, 1349, 1350, 1351, 1352, 1353, 1354, 1355, 1356, 1357, 1358, 1359, 1360, 1361, 1362, 1363, 1364, 1365, 1366, 1367, 1368, 1369, 1370, 1371, 1372, 1373, 1374, 1375, 1376, 1377, 1378, 1379, 1380, 1381, 1382, 1383, 1384, 1385, 1386, 1387, 1388, 1389, 1390, 1391, 1392, 1393, 1394, 1395, 1396, 1397, 1398, 1399, 1400, 1401, 1402, 1403, 1404, 1405, 1406, 1407, 1408, 1409, 1410, 1411, 1412, 1413, 1414, 1415, 1416, 1417, 1418, 1419, 1420, 1421, 1422, 1423, 1424, 1425, 1426, 1427, 1428, 1429, 1430, 1431, 1432, 1433, 1434, 1435, 1436, 1437, 1438, 1439, 1440, 1441, 1442, 1443, 1444, 1445, 1446, 1447, 1448, 1449, 1450, 1451, 1452, 1453, 1454, 1455, 1456, 1457, 1458, 1459, 1460, 1461, 1462, 1463, 1464, 1465, 1466, 1467, 1468, 1469, 1470, 1471, 1472, 1473, 1474, 1475, 1476, 1477, 1478, 1479, 1480, 1481, 1482, 1483, 1484, 1485, 1486, 1487, 1488, 1489, 1490, 1491, 1492, 1493, 1494, 1495, 1496, 1497, 1498, 1499, 1500, 1501, 1502, 1503, 1504, 1505, 1506, 1507, 1508, 1509, 1510, 1511, 1512, 1513, 1514, 1515, 1516, 1517, 1518, 1519, 1520, 1521, 1522, 1523, 1524, 1525, 1526, 1527, 1528, 1529, 1530, 1531, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1539, 1540, 1541, 1542, 1543, 1544, 1545, 1546, 1547, 1548, 1549, 1550, 1551, 1552, 1553, 1554, 1555, 1556, 1557, 1558, 1559, 1560, 1561, 1562, 1563, 1564, 1565, 1566, 1567, 1568, 1569, 1570, 1571, 1572, 1573, 1574, 1575, 1576, 1577, 1578, 1579, 1580, 1581, 1582, 1583, 1584, 1585, 1586, 1587, 1588, 1589, 1590, 1591, 1592, 1593, 1594, 1595, 1596, 1597, 1598, 1599, 1600, 1601, 1602, 1603, 1604, 1605, 1606, 1607, 1608, 1609, 1610, 1611, 1612, 1613, 1614, 1615, 1616, 1617, 1618, 1619, 1620, 1621, 1622, 1623, 1624, 1625, 1626, 1627, 1628, 1629, 1630, 1631, 1632, 1633, 1634, 1635, 1636, 1637, 1638, 1639, 1640, 1641, 1642, 1643, 1644, 1645, 1646, 1647, 1648, 1649, 1650, 1651, 1652, 1653, 1654, 1655, 1656, 1657, 1658, 1659, 1660, 1661, 1662, 1663, 1664, 1665, 1666, 1667, 1668, 1669, 1670, 1671, 1672, 1673, 1674, 1675, 1676, 1677,



AB The title compds. I [wherein R1 and R2 = independently H, halo, alkyl, (un)substituted alkoxy, amino, alkylamino(alkoxy), dialkylamino(alkoxy), NHC(=O)-alkyl, O-alkylene-CO2R, or (hetero)cyclylalkoxy; or R1 and R2 together form a ring; R3 = H, alkyl, or (un)substituted PhCH2; R4 and R5 = independently H, (un)substituted alkyl, halo, CO2R, CONH2, CONR-alkyl, (un)substituted (hetero)cyclyl(carbonyl), alkyl-CO, or CN; or R3 and R4 together are alkylene or oxo; R5 = H, alkyl, (alkylene)CO2R, CONH2, CONR-alkyl, alkyl-CO, (un)substituted (hetero)cyclyl(hydrocarboxyl), (hetero)cyclyl(alkylene)(carbonyl), CO2-alkylene-(hetero)cyclyl, or carbamoyl, etc.; n = 0-1; with proviso] and pharmaceutically acceptable salts thereof are prepared as PDE IV inhibitors. I are useful for the prevention and treatment of respiratory tract diseases, asthma, and chronic obstructive pulmonary diseases (COPD) (no data). For example, a THF solution of 6-(3,4-dimethoxyphenyl)pyridine-2-carboxylic acid (prepa given) was treated with oxalic chloride, followed by the addition of 4-(4-methoxyphenyl)piperazine (prepa given) in the presence of pyridine to afford the piperazine II. II showed IC50 of 412 nM against PDE IV.

IT 5368-28-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of phenylpyridinecarboxylpiperazine derivs. as PDE IV inhibitors)

RN 5368-28-5 CAPLUS

CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

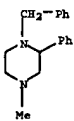
L7 ANSWER 18 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 2002:86916 CAPLUS  
DOCUMENT NUMBER: 137:370108  
TITLE: Methylation-debenzylation process for preparing 1-methyl-3-phenylpiperazine from 1-benzyl-2-phenylpiperazine and formaldehyde  
INVENTOR(S): Rao, Davuluri Ramamohan; Rao, Chunduru Sankara;



IT 23174-98-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(methylation-debenzylation process for preparing 1-methyl-3-phenylpiperazine from 1-benzyl-2-phenylpiperazine and formaldehyde with intermediate preparation of)

RN 23174-98-3 CAPLUS

CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 2002:767304 CAPLUS  
DOCUMENT NUMBER: 138:362130  
TITLE: Synthesis and NK1/NK2 binding activities of a series of diacyl-substituted 2-aryl piperazines  
AUTHOR(S): Blythin, David J.; Chen, Xiao; Piwnicki, John J.; Shih, Meng-Yang; Shue, Ho-Jane; Anthes, John C.; McPhail, Andrew T.  
CORPORATE SOURCE: Chemical Research Department, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3161-3165  
CODEN: BMCLEB; ISSN: 0960-894X  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 138:362130

AB The synthesis and binding affinity for NK1 and NK2 receptors of a series of diacyl substituted 2-aryl piperazines are described. SAR evaluation led to one racemic derivative as an apparent dual inhibitor. Chiral chromatog. separation of racemic derivative led to the observation that NK1 activity was shown by one enantiomer and NK2 activity was shown by the other enantiomer. X-ray crystallog. anal. of the crystalline di-BOC derivative of the NK2 active piperazine showed that the 2R configuration was associated with NK2 activity. Further derivatization indicated that dual NK1/NK2 activity could be built into the 2R series.

IT 5271-26-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and NK1/NK2 binding structure-activities of a series of

PATENT ASSIGNEE(S): Sreenivasulu, Pamjula  
SOURCE: Neuland Laboratories Limited, India  
PCT Int. Appl., 9 pp.  
CODEN: PIXXDJ  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090339	A1	20021114	WO 2002-1M117	20020506
W:	AS, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, ES, ES, FI, GB, GD, GE, GR, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPL. INFO.: IN 2001-MA364 A 20010508  
OTHER SOURCE(S): CASREACT 137:370108

AB A process for preparing 1-methyl-3-phenyl-piperazine, which comprises: (i) conducting a regioselective methylation via mixing 1-benzyl-2-phenylpiperazine with a formic acid solution while stirring and then adding a formaldehyde solution and heating the mixture to 70-80 ° for 50-70 min; (ii) reheating the obtained solution of step (i) to 90-95° for 50-70 min; (iii) checking the obtained mass of step (ii) for the absence of the starting material and treating the mixture with sodium hydroxide solution while stirring for 50-70 min at <25° and filtering; (iv) washing the product of step (iii) with water and drying to obtain 1-benzyl-4-methyl-2-phenylpiperazine; (v) the step (iv) product is subjected to a hydrogenolytic debenzylation using a Pd/C catalyst at a hydrogen pressure of 3.5-4.0 kg/cm2 for 6-10 h followed by product workup.

IT 5368-33-2, 1-Benzyl-2-phenylpiperazine  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(methylation-debenzylation process for preparing 1-methyl-3-phenylpiperazine from 1-benzyl-2-phenylpiperazine and formaldehyde)

RN 5368-33-2 CAPLUS

CN Piperazine, 2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT 5271-27-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(methylation-debenzylation process for preparing 1-methyl-3-phenylpiperazine from 1-benzyl-2-phenylpiperazine and formaldehyde)

RN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

diacyl-substituted 2-aryl piperazines)

RN 5271-24-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



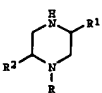
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 2002:368461 CAPLUS  
DOCUMENT NUMBER: 136:369741  
TITLE: A novel method for preparation of piperazine and its derivatives  
INVENTOR(S): Sebastian, Sonny; Patel, Hetal Virendra; Themnati, Rajasamrat  
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Ltd., India  
SOURCE: PCT Int. Appl., 23 pp.  
CODEN: PIXXDJ  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038552	A1	20020516	WO 2001-1M129	20010629
W:	AS, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, ES, ES, FI, GB, GD, GE, GR, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001078669	A5	20020521	AU 2001-78669	20010629
BE 1013317	A6	20011106	BE 2001-513	20010727
CH 692342	A	20020515	CH 2001-1428	20010802
US 2002095038	A1	20020718	US 2001-37309	20011025
US 6603803	B2	20030805		

PRIORITY APPL. INFO.: IN 2000-MU994 A 20001107  
WO 2001-1M129 W 20010629

OTHER SOURCE(S): CASREACT 136:369741, MARPAT 136:369741  
GI



AB Compds. I [R = H, C1-6 alkyl, phenyl-C1-4 alkyl; R1 = H, Me, (un)substituted phenyl; R2 = H, Me, fluoromethyl] useful as starting

materials for preparation of pharmaceutically active compds. are prepared by reacting 21COCOCGR with H2NCH2CH2NHR to give 3,4-dihydropiperazine-2-one and its derive., followed by a reducing agent to yield I. Thus, 1-methyl-3-phenylpiperazine was prepared and used as starting material for preparation of 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino(2,1-a)pyrido(2,3-c)[1,2]benzotetrapine.

IT 5271-27-2P 1-methyl-3-phenylpiperazine  
 RL: IMP (Industrial manufacture), RCT (Reactant), PREP (Preparation), RACT (Reactant or reagent)  
 (preparation of piperazine derive. as starting materials for preparation of pharmaceutically active compds.)  
 EN 5271-27-2 CAPLUS  
 CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STM  
 ACCESSION NUMBER: 2001:935558 CAPLUS  
 DOCUMENT NUMBER: 136:53575  
 TITLE: Preparation of substituted nitrocatechols as catechol-O-methyltransferase inhibitors  
 INVENTOR(S): Learmenath, David Alexander; Soares da Silva, Patricio  
 PATENT ASSIGNEE(S): Portela & CA SA, Port.  
 SOURCE: PCT Int. Appl., 29 pp.  
 CODEN: PIKX02  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098251	A1	200111227	WO 2001-GB2777	20010621
W: AS, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM				
EW: GM, GR, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TO				
GB 2363792	A1	20020109	GB 2000-15225	20000621
CA 2351129	AA	20011221	CA 2001-2351129	20010620
US 2003060472	A1	20030327	US 2001-085854	20010620
EP 1167342	A1	20020102	EP 2001-305391	20010621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

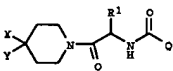
PRIORITY APPLN. INFO.: GB 2000-15225 A 20000621  
 OTHER SOURCE(S): MARPAT 136:53575  
 GI

SOURCE: PCT Int. Appl., 220 pp.  
 CODEN: PIKX02  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070708	A1	20010927	WO 2001-US8935	20010320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
EW: GM, GR, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TO				
CA 2403686	AA	20010927	CA 2001-2403686	20010320
US 2002019523	A1	20020214	US 2001-812945	20010320
US 6458799	B2	20021001		
EP 1268449	A1	20030102	EP 2001-922501	20010320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MX, CY, AL, TR				
JP 2003520088	T2	20030924	JP 2001-568918	20010320
US 2000-191442P	P		US 2000-191442P	20000323
US 2000-242265P	P		US 2000-242265P	20001020
WO 2001-US8935	W			20010320

PRIORITY APPLN. INFO.: JP 2001-568918 P 20000323  
 US 2000-242265P P 20001020  
 WO 2001-US8935 W 20010320

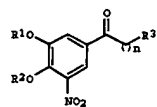
OTHER SOURCE(S): MARPAT 135:272990  
 GI



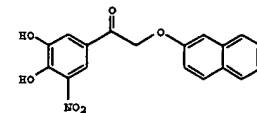
AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl, R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocycloalkyl(alkyl), cyano(alkyl), aminoalkyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocycloalkyl(alkyl), heteroaryl(alkyl)], were prepared as melanocortin-4 receptor (MC-4R) agonists. Thus, capsule formulations containing title compound (II) were prepared. Representative I activated MC-4R with IC50<1 nM. I are claimed for the treatment of obesity, diabetes, and sexual dysfunction including erectile dysfunction and female sexual dysfunction.

IT 363188-90-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of piperazinylcarboxylaminomethylcarboxylpiperidines as melanocortin-4 receptor agonists)

EN 363188-90-3 CAPLUS  
 CN 2-Piperazinecarboxamide, N-[(1R)-2-(4-cyclohexyl-4-[[[1,1-dimethyl-2-ethylamino]carbonyl]-1-piperidinyl]-1-[(4-fluorophenyl)methyl]-2-oxoethyl]-4-methyl-3-phenyl- (9CI) (CA INDEX NAME)



I



II

AB Title compds. I [R1-2 = H, groups hydrolyzable under physiol. pH, alkanoyl, aroyl, alkyl, arylsulfonyl, etc.; n = 1-2; R3 = OR4, SR5, NR6, alkylamino, etc.; R4 = aryl; R5 = (hetero)aryl; R6 = (cyclo)alkyl, heterocycloalkyl, alkylaryl, etc.] were prepared. For example, 2-naphthol (3 mol equivalent) was alkylated with 2-chloro-1-(3,4-dihydroxy-5-nitrophenyl)ethanone (IMP, K2CO3, 100°C, 1 h) to give II. Administration of II evaluated at 1 h was shown to inhibit mouse-liver catechol-O-Me transferase (COMT) 17% and brain COMT 83% vs. control. I are useful in the treatment of some central and peripheral nervous system disorders.

IT 383184-92-7, 2-(Chlorophenyl)piperazine hydrochloride  
 RL: RCT (Reactant), RACT (Reactant or reagent)  
 (reactant; preparation of substituted nitrocatechols as catechol-O-methyltransferase inhibitors)  
 EN 383184-92-7 CAPLUS  
 CN Piperazine, 2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

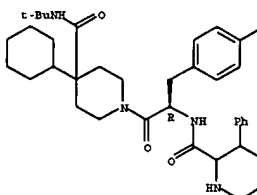


● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STM  
 ACCESSION NUMBER: 2001:713326 CAPLUS  
 DOCUMENT NUMBER: 135:272990  
 TITLE: Preparation of piperazinylcarboxylaminomethylcarboxylpiperidines as melanocortin-4 receptor agonists  
 INVENTOR(S): Palucki, Brenda L.; Barakat, Khaled J.; Guo, Liangqin; Lei, Yangjie; Margund, Ravi P.; Park, Min K.; Pollard, Patrick G.; Sebbat, Iyassu K.; Ye, Zhixiang  
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STM  
 ACCESSION NUMBER: 2001:326870 CAPLUS  
 DOCUMENT NUMBER: 134:326545  
 TITLE: Preparation of 1-methyl-3-phenylpiperazine as intermediate for mirtazapine  
 INVENTOR(S): Maeda, Chiharu; Iseki, Eiichi; Yoshikawa, Sadanobu  
 PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.  
 CODEN: JKKYAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001122863	A2	20010508	JP 1999-307698	19991028
JP 1999-307698			JP 1999-307698	19991028

PRIORITY APPLN. INFO.: CASREACT 134:326545

AB Title compound is prepared by the condensation of phenylglyoxal with ethylenediamine, reduction of the condensation products, and methylation of 2-phenylpiperazine. Phenylglyoxal was reacted with ethylenediamine in EtOH at 45°C for 3 h and reduced with NaBH4 at 20-30°C for 21 h to give 81.4% 2-phenylpiperazine, which was methylated with Me2SO4 in the presence of KOH in PhMe at 15-20°C for 1.5 h to give 67.1% 1-methyl-3-phenylpiperazine.

IT 5271-26-1E, 2-Phenylpiperazine  
 RL: RCT (Reactant), SPN (Synthetic preparation), PREP (Preparation), RACT (Reactant or reagent)  
 (preparation of methylphenylpiperazine by condensation of phenylglyoxal with ethylenediamine, reduction, and methylation)

EN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 24 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM

ACCESSION NUMBER: 2001:265403 CAPLUS

DOCUMENT NUMBER: 134:295839

TITLE: Preparation of 2-phenylpiperazine-1-carboxylic acid

INVENTOR(S): Alvaro, Giuseppe; Di Fabio, Romano; Giovannini, Riccardo; Guerico, Giuseppe; St. Denis, Yves; Ursini, Antonella

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXND2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025219	A2	20010412	WO 2000-EP9722	20001005
WO 2001025319	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG				
CA 2386515	AA	20010412	CA 2000-2386515	20001005
EP 1218359	A2	20020703	EP 2000-969414	20001005
EP 1218359	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
TR 200200936	T2	20020723	TR 2002-200200936	20001005
BR 2000014541	A	20020917	BR 2000-14541	20001005
JP 2003511377	T2	20030325	JP 2001-528165	20001005
AU 768780	B2	20040108	AU 2000-79139	20001005
NZ 518144	A	20040430	NZ 2000-518144	20001005
AT 270664	E	20040715	AT 2000-969414	20001005
EP 1454901	A1	20040908	EP 2004-76650	20001005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY				
EP 1460066	A1	20040922	EP 2004-76652	20001005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY				
ES 2229277	T3	20050216	ES 2000-969414	20001005
TW 225485	B1	20041221	TW 2000-89121014	20001007
ZA 2002002589	A	20020703	ZA 2002-2589	20020403
NO 2002001637	A	20020606	NO 2002-1637	20020405
US 2003028021	A1	20030206	US 2002-190170	20020703
US 6642240	B2	20031104		
US 2004048862	A1	20040311		
US 2004209893	A1	20041021		
PRIORITY APPL. INFO.:				
OTHER SOURCE(S):				
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to piperazine derivs. I [wherein: R = halo, C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = H, C1-4 alkyl, C2-6 alkenyl, C3-7 cycloalkyl, or NR1CR2 = 5- to 6-membered heterocyclyl; R3 = CF3, C1-4 alkyl, C1-4 alkoxy, CF3O, or halo; R4 = H, (CH2)qR7 or (CH2)qCO(CH2)pr7; R5 = H, C1-4 alkyl or CO2R6; R6 = H, CH, NH2, NMe2, 5-membered heterocyclyl containing 1-3 H/O/S or 6-membered heterocyclyl containing 1-3 N atoms; R7 = H, CH, or NR8R9 wherein R8 and R9 = H or C1-4 alkyl (un)substituted by OH or by NH2; R10 = H, C1-4 alkyl, or R10 and R2 form C3-7 cycloalkyl; n = 0-3; p, r = 0-4; q = 1-4; provided that, when NR1CR2 = 5- to 6-membered heterocyclyl, then (i) n = 1 or 2; (ii) when n = 1, R = F; and (iii) when n = 2, both R = F and pharmaceutically acceptable salts and solvates thereof. The compds. are potent and specific antagonists of tachykinins, including substance P and other neurokinins. Examples include 38 syntheses, 82 preps. of intermediates, 4 standard formulations, and 2 bioassays. For instance, (+)-(S)-3-(4-fluoro-2-methylphenyl)piperazin-2-one (preparation given) was treated with triphosgene and amidated with 3,5-(F3C)2C6H3CH2NH2 to give 2 diastereomeric amides. Separation of the (5S)-diastereomer by flash chromatog. and reduction of the ring oxo group with BH3.THF gave title compound II, isolated as the acetate salt (III). Using the gerbil foot-tapping model for reversal of an NK1 agonist, III had an oral ED50 of 0.04 mg/kg.

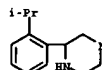
IT 334477-62-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of phenylpiperazinecarboxylic acid benzylamides as tachykinin antagonists)

BN 334477-62-2 CAPLUS

CN Piperazine, 2-[2-(1-methylethyl)phenyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

IT 5368-28-5, 3-Phenylpiperazin-2-one

RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of phenylpiperazinecarboxylic acid benzylamides as tachykinin antagonists)

BN 5368-28-5 CAPLUS

CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 25 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM

ACCESSION NUMBER: 2001:265272 CAPLUS

DOCUMENT NUMBER: 134:280862

TITLE: Process for the preparation of a piperazine derivative

INVENTOR(S): Maeda, Chiharu; Iishi, Eiichi; Wang, Weigi; Imamiya, Yoshiyuki

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXND2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025185	A1	20010412	WO 2000-JP5432	20000814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG				
CA 2351538	AA	20010405	CA 2000-2351538	20000927
WO 2001023345	A1	20010405	WO 2000-JP6650	20000927
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EP 1136470	A1	20010926	EP 2000-962874	20000927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 751628	B2	20020822	AU 2000-74455	20000927
US 6495685	B1	20021217	US 2000-697140	20001027
PRIORITY APPL. INFO.:				
OTHER SOURCE(S):				
GI				

presence of a base and an alkali metal halide in an aprotic polar organic solvent. This piperazine derivative I and its oxalate are useful as intermediates for the preparation of mirtazapine. Thus, 11.4 kg N-methylethanolamine was added dropwise to a solution of 20 kg styrene oxide in 38 kg DMF at approx. 80°, stirred at approx. 80° for 3 h, and cooled to room temperature to give a DMF solution of N-(2-hydroxyethyl)-N-methyl-2-hydroxy-2-phenylethylamine which was added dropwise to a solution of 45 kg SOCl2 in 67.4 kg toluene at 0-25°, stirred at 45-55° for 2 h, cooled at 525°, treated dropwise with 95 kg H2O and then with 30 weight% aqueous KOH at 0-25°, and left to stand for phase separation. The organic and aqueous phase were separated and the aqueous phase was extracted with 55 kg toluene, followed by combining the extract and the organic phase, drying over 4.8 kg MgSO4, treating with 4.8 kg activated clay and filtration, and washing with 19.9 kg PMe to give a toluene solution of N-(2-chloroethyl)-N-methyl-2-chloro-2-phenylethylamine (II). To the toluene solution was introduced 5.5 kg HCl(g) at 10-35° and stirred at 20-25° for 2 h and the precipitated crystals were filtered and washed with 69 kg toluene

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

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ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc

(2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8 g 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum

ether 36% I (3.14 g, 97.1% purity).

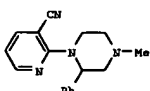
IT 5271-27-2P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylphenylpiperazinyl)cyanopyridine as intermediate for mirtazapine)

BN 5271-27-2 CAPLUS

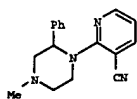
CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



AB A process for the preparation of a piperazine derivative, namely 2-(4-methyl-3-phenylpiperazin-1-yl)-3-cyanopyridine (I), comprises reacting 1-methyl-3-phenylpiperazine with 2-chloro

LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023345	A1	20010405	WO 2000-JP6650	20000927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, ES, FI, GE, GR, GU, HK, HM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, NO, NZ, PL, PT, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001025185	A1	20010412	WO 2000-JP5432	20000814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, ES, FI, GE, GR, GU, HK, HM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, NO, NZ, PL, PT, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315150	A1	20010926	CA 2000-025538	20000627
EP 1136470	A1	20010926	EP 2000-962874	20000927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 751629	B2	20020822	AU 2000-744455	20000927
PRIORITY APPLN. INFO.:			JP 1999-280378	A 19990309
			WO 1999-JP5432	A 20000814
			WO 2000-JP6650	A 20000927
OTHER SOURCE(S):	CASREACT	134:266325		
GI				



**AB** A process for the preparation of a piperazine derivative represented by formula (I), namely 2-(4-methyl-2-phenylpiperazin-1-yl)-3-cyanopyridine, comprises reacting 1-methyl-3-phenylpiperazine (II) with 2-chloro-3-cyanopyridine (III) in the presence of a base and an alkali metal halide in an aprotic polar organic solvent. This piperazine derivative and its oxalate are useful

intermediates for the preparation of mirtazapine. Thus, styrene oxide underwent addition reaction with N-methylphenolamine in DMF at 80° for 3 h to give a solution of N-(2-hydroxyethyl)-N-methyl-2-hydroxy-2-phenylethylamine which was treated dropwise with a solution of SOCl<sub>2</sub> in toluene at 0-25°, stirred at 45-55° for 2 h, cooled to 52°, and treated dropwise with water and then with 30 weight % NaOH at 20-25° to give, after workup, a toluene solution of N-(2-chloroethyl)-N-methyl-2-chloro-2-phenylethylamine. The latter solution

given: i-Pr, Ph, Me, Ph, Me, H, H, H, resp.) have been studied using NMR spectral techniques and semielemental MO calcs. Each of the diformylpyrrolasines 9-11 have been found to exist as an equilibrium mixture of four rotamers resulting from the restricted N-C rotation at the two N-C=O bonds. All the four rotamers (anti-anti, anti-syn, syn-anti, syn-syn) of 9 were found to adopt the twist-boat (B4) conformations. Similarly all the four rotamers of 10 prefer the twist-boat (B4) conformation. On the other hand the diformylpyrrolasine 10 has been found to adopt different ring conformations depending upon the N-CHO rotameric states (B4 for the rotamer A, B3 in the cases of rotamers B and D, and CA for the rotamer C). The A1,3-strain and the resonance energy (arising from the delocalization of the lone pair of electrons on the nitrogen) have been found to be the most important factors in determining the conformational preferences of all the pyrrolasine derivatives and semielemental MO calcs. supports the conformational preferences and the nature of the conformational equilibrium derived from the NMR results.

IT 81602-00-8  
EL: RCT (Reactant); RACT (Reactant or reagent)  
(formylation; influence of competing Al,3-strain on the conformational  
preferences of N1,N4-diformylpiperazines)  
RN 81602-00-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

**Relative stereochemistry.**



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2000:756684 CAPLUS  
DOCUMENT NUMBER: 123:321901  
INVENTOR(S): Metal synthesis of piperasine ring  
PATENT ASSIGNER(S): Doltzky, Ben-Zion  
Teva Pharmaceutical Industries Ltd., Israel; Teva  
Pharmaceuticals Usa, Inc.  
PCT Int. Appl., 19 Pp.  
SOURCE: CODEN: FIKX22  
Patent  
DOCUMENT TYPE: English  
LANGUAGE: FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATIENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000063185	AA	20001026	WO 2000-US9418	20000807
W, AB	AL, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CZ, DE, DK, DM, DZ, EE, ES, FI, FG, GE, GR, HA, HB, HC, HD, HE, HF, HG, HH, HI, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LZ, LX, LY, MA, MD, MG, MK, MN, MX, MY, NZ, PL, PT, RU, RO, RS, SE, SI, SK, SL, SM, SN, SR, SS, SU, SV, SZ, TH, TJ, TM, TR, TW, UG, UA, UK, US, UZ, VU, VY, ZA	CH, CR, DE, ES, FI, FR, GB, GR, HA, HB, HC, HD, HE, HF, HG, HH, HI, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LZ, LX, LY, MA, MD, MG, MK, MN, MX, MY, NZ, PL, PT, RU, RO, RS, SE, SI, SK, SL, SM, SN, SR, SS, SU, SV, SZ, TH, TJ, TM, TR, TW, UG, UA, UK, US, UZ, VU, VY, ZA	20000407	
EW: GE, GM, GR, HA, HB, HC, HD, HE, HF, HG, HH, HI, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LZ, LX, LY, MA, MD, MG, MK, MN, MX, MY, NZ, PL, PT, RU, RO, RS, SE, SI, SK, SL, SM, SN, SR, SS, SU, SV, SZ, TH, TJ, TM, TR, TW, UG, UA, UK, US, UZ, VU, VY, ZA	AA	20001026	WO 2000-373703	20000407
CA 2370348	AA	20001026	WO 2000-373703	20000407

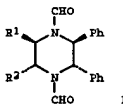
was treated HCl(g) 10-35% and stirred at 20-25° for 2 h to give N-[2-(chloromethyl)-N-methyl-2-chloro-2-phenylethylamine hydrochloride which was stirred with a mixture of Bu<sub>4</sub>NBr, aqueous NH<sub>3</sub>, toluene, and DMF at 40-44° for 2 h, treated with 25 weight % NaOH, and stirred at 45-47° for 2 h to give, after workup, 58.70 II. A mixture of II, III, KI, and Et<sub>3</sub>N in DMF was stirred at 115-120° for 10 h and then at 135° to give 13.3% III and the stirrer was stopped and the mixture at 135-127° for 5 h to give, after workup and salt formation with oxalic acid, 61.9% I, oxalic acid.

IY	Maleic acid, 1-methyl-oxalic acid.
RN	5271-27-26 Piperazine, 1-methyl-3-phenyl-
RL	LMF (Industrial manufacture), RCT (Reactant), SPN (Synthetic preparation), PREP (Preparation), RACT (Reagent or reagent) (preparation of methylenephosphorazinyl)cyanopyridine by chlorination of N-(hydroxyethyl)-N-methylhydroxyphenylethylamine and cyclization to methylenephosphorazine followed by condensation with chlorocyanopyridine)
RN	5271-27-2 CAPLUS
CN	Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

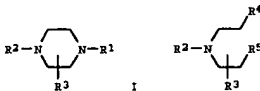
L7 ANSWER 27 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:76725 CAPLUS  
DOCUMENT NUMBER: 134:251986  
TITLE: Influence of competing Al,3-strain on the  
conformational preferences of N,N4-  
diformylpiperazines  
AUTHOR(S): Jayaraman, R.; Murugadoss, R.  
CORPORATE SOURCE: Department of Chemistry, Bharathidasan University,  
Tiruchirappalli, 620 024, India  
SOURCE: Indian Journal of Chemistry, Section B: Organic  
Chemistry Including Medicinal Chemistry (2000),  
39B(11), 826-835  
CODEN: IJSEDB; ISSN: 0376-4699  
PUBLISHER: National Institute of Science Communication, CSIR  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 134:251986  
GI



AB The conformational preferences of N1,N4-di-formylpiperazines 9-12 (I; R1,R2

US	6339156	B1	20020115	US	2000-545011		20000407
TR	2001030305	T2	20020121	TR	2001-200103035		20000407
EP	1178972	A	20020213	EP	GR 2001-921933		20000407
R : AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO							
JF	200452234	L2	20020210	JF	2000-613277		20000407
AU	777105	B2	20004920	AU	2000-42190		20000407
US	2002035256	A1	20020321	US	2001-939406		20010824
US	6852855	B2	20005208				
ZA	2001008480	A	20021115	ZA	2001-0480		20011016
HR	2001000759	A	20030228	HR	2001-759		20011018
PRIORITY APPLN. INFO. :				US	1999-130048P	P	19990419
				US	2000-545011	YK	20000407
				WO	2000-US9418	W	20000407
OTHER SOURCE(S) :				CASREACT	133:321901;	MARPAT	133:321901
OI							

OTHER SOURCE(S): CASREACT 133:321901, MARPAT 133:321901  
GI



AB A novel process for preparing the compds I (R1 = (un)substituted alkyl, alkoxy, aryl, aryloxy, aryloxyalkyl; R2 = (un)substituted alkyl, alkoxy, aryl, aryloxy, aryloxyalkoxy, tosyl, formyl, acetyl, amino; R3 = (un)substituted alkyl, alkoxy, aryl, aryloxy, aryloxyalkyl), comprising the step of reacting the compound II (R4, R5 = F, Cl, Br, I) with H2NR1, is disclosed. The compds. I are useful as intermediates in the synthesis of the antidepressant mirtazapine and other tetracyclic compds.

the antidepressant mirtazapine and other tetracyclic compou.  
IT 5271-27-2P  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP  
(Preparation)  
(novel synthesis of piperazine ring)  
RN 5271-27-2 CAPIUS  
CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

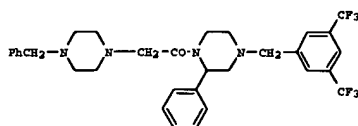


L7 ANSWER 39 OF 120 CAPLUS COPYRIGHT 2005 ACS COM STN  
ACCESSION NUMBER: 2000:725471 CAPLUS  
DOCUMENT NUMBER: 133:281794  
TITLE: Preparation of aminopyrimidines as sorbitol  
dehydrogenase inhibitors  
INVENTOR(S): Chu-moy, Margaret Yuhua; Murry, Jerry Anthony;  
Myland, Barbara Lakshmi; Zembrowski, William James  
PATENT ASSIGNER(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 328 pp.



US 1996-663880 A2 19960614  
US 1995-432739 A 19950502  
US 1995-3084P P 19950831  
US 1996-706016 A 19960830  
WO 1997-US14709 W 19970828

OTHER SOURCE(S): MARPAT 130:252385  
GI



AB The title compds. were prepared and the NK1 and NK2 antagonist activity determined. E.g., piperazine derivative I was prepared. These compds. are useful in the treatment of chronic airway diseases such as asthma.  
IT 5271-26-1P, 2-Phenylpiperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of piperazine derivs. as NK1 and NK2 antagonists)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1998:564199 CAPLUS  
DOCUMENT NUMBER: 129:189341  
TITLE: Preparation of piperazines as neurokinin antagonists  
INVENTOR(S): Shue, Ho-Jane; Shih, Meng-Yang; Blythin, David J.; Chen, Xiao; Tora, Wing C.; Piwnicki, John J.; McCormick, Kevin D.  
PATENT ASSIGNEE(S): Schering Corp., USA  
SOURCE: U.S., 92 pp., Cont.-in-part of U. S. 5,719,156.  
CODEN: USYXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5795894	A	19980810	US 1996-663880	19960614
US 5719156	A	19980217	US 1995-432739	19950502
US 5798359	A	19980825	US 1995-451113	19950525
CN 1189829	A	19980805	CN 1996-195171	19960501
CN 1111528	B	20030610		

AB The title compds. [I; u = 0-2; yr = 1-3 (with the proviso that no more than one R1 is other than H); R1 = H, C1-6 alkyl, hydroxy(C1-6 alkyl), etc.; Ar1 = (un)substituted pyridyl, Ph, naphthyl; Ar2 = (un)substituted Ph; Z = (un)substituted II, III, etc.) and their salts, neurokinin antagonists useful in the treatment of chronic airway diseases such as asthma and bronchospasm, were prepared. Thus, reaction of [3,5-bis(trifluoromethyl)benzoyl]-3-(3,4-dichlorophenyl)piperazine with BrCH2COCl in the presence of (iPr)2NEt in CH2Cl2 followed by the addition of 4-amino-1-benzylpiperidine afforded 62w the title compound IV which showed Ki of 4.9 nM and 11.4 nM for NK1 and NK2 binding, resp.  
IT 5271-26-1P, 2-Phenylpiperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of piperazines as neurokinin antagonists)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



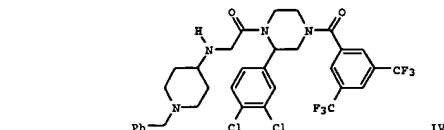
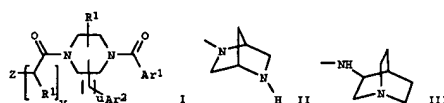
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 34 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1998:163574 CAPLUS  
DOCUMENT NUMBER: 128:230391  
TITLE: Preparation of N-(piperidinoacetyl)piperazines and analogs as neurokinin antagonists  
INVENTOR(S): Shue, Ho-Jane; Shih, Meng-Yang; Blythin, David J.; Chen, Xiao; Piwnicki, John J.; McCormick, Kevin D.  
PATENT ASSIGNEE(S): Schering Corporation, USA  
SOURCE: PCT Int. Appl., 85 pp.  
CODEN: PIXKD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808826	A1	19980305	WO 1997-US14709	19970828
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, ND, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM				
HW: GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5892039	A1	19990406	US 1996-706016	19960830
CA 2264005	AA	19980305	CA 1997-2264005	19970828
AU 9740800	A1	19980319	AU 1997-40800	19970828
EP 927170	A1	19990707	EP 1997-938490	19970828
EP 927170	B1	20031008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO				
JP 2000516956	T2	20001219	JP 1998-511732	19970828
AT 251614	E	20031015	AT 1997-938490	19970828
HX 1010265	A1	20040520	HX 1999-103192	19990726

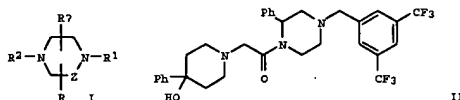
CA 2228370 AA 19970306 CA 1996-2228370 19960829  
CA 2228370 C 20021001  
WO 9708166 A1 19970306 WO 1996-1B1018 19960829  
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, ND, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, HW: IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  
AU 9669979 A1 19970319 AU 1996-69979 19960829  
AU 708834 B2 19990812  
EP 850238 A1 19980701 EP 1996-931188 19960829  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI  
JP 10511105 T2 19981027 JP 1997-510069 19960829  
JP 3447745 B2 20030916  
CN 1200120 A 19981125 CN 1996-197720 19960829  
CN 1111529 B 20030610  
US 5869489 A 19990209 US 1996-703154 19960829  
EP 9610277 A 19990706 EP 1996-10277 19960829  
JP 2000344766 A2 20001212 JP 2000-153870 19960829  
JP 3215970 B2 20020819  
IL 123112 A1 20010430 IL 1996-123112 19960829  
AT 202776 E 20010715 AT 1996-931188 19960829  
ES 2158345 T3 20010901 ES 1996-931188 19960829  
US 5892039 A 19990406 US 1996-706016 19960830  
NO 9800848 A 19980430 NO 1998-048 19980227  
US 5981520 A 19991109 US 1998-99221 19980617  
GB 3036675 T3 20011231 GR 2001-401532 20010920  
PRIORITY APPLN. INFO.: US 1995-432739 A2 19950502  
US 1995-3084P P 19950831  
WO 1996-US5660 W 19960501  
US 1996-706016 A 19960830  
JP 1997-510069 A3 19960829  
WO 1996-1B1018 W 19960829

OTHER SOURCE(S): MARPAT 129:189341  
GI



PRIORITY APPLN. INFO.: US 1996-706016 A 19960830  
WO 1996-US5660 W 19960501  
US 1996-663880 A2 19960614  
WO 1997-US14709 W 19970828

OTHER SOURCE(S): MARPAT 128:230391  
GI



AB Title compds. [I; R = (CH2)uAr2; R1 = C(X)(CH2)uAr1; R2 = [C(X)]m(CH2)uR3; R3 = cycloalkylamino, acycloalkyl, etc.; Ar1, Ar2 = (un)substituted (hetero)aryl, R = H or (un)substituted alkyl; R' = H, (hydroxy)alkyl, alkoxyalkyl, etc.; X = O, S, H2, (alkyl)imino, etc.; Z = bond, CH2, CH2CH2, 1,u = 0-2; m = y = 1; m = 2 and y = 0 were prepared. Thus, chloropyrazine was arylated by PhMgBr and the reduced product N-alkylated by 3,5-(F3C)2C6H3CH2Br to give Ph21CH2C6H3(CF3)2-3,5 (Z1 = piperazine-2,4-diyl) which was N-acylated by BrCH2COBr and the product eliminated by 4-hydroxy-4-phenylpiperidine to give title compound II. Data for biol. activity of I were given.  
IT 5271-26-1P, 2-Phenylpiperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of N-(piperidinoacetyl)piperazines and analogs as neurokinin antagonists)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1998:126258 CAPLUS  
DOCUMENT NUMBER: 128:192669  
TITLE: Palladium catalyzed indolization of 2-halo- or 2-(trifluoromethyl)sulfonyl aniline and acyl silane derivatives  
INVENTOR(S): Chen, Cheng-Yi; Larsen, Robert D.  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Chen, Cheng-Yi; Larsen, Robert D.  
SOURCE: PCT Int. Appl., 90 pp.  
CODEN: PIXKD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

IT 5368-28-5, 3-Oxo-2-phenylpiperazine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of heterocyclyl-substituted azetidines, pyrrolidines and  
 piperidines as selective agonists of 5-HT<sub>1</sub>-like receptors)

BN 5368-20-5 CAPLUS  
CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 38 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1997:38766 CAPLUS  
DOCUMENT NUMBER: 126:59974  
TITLE:

Preparation of 1-benzoyl-2-[(4-piperidinylamino)acetyl]piperazines and analogs as neurokinin antagonists  
INVENTOR(S): Shue, Ho-Jane; Shih, Meng-Yang; Blythin, David J.; Chen, Xiao; Tse, Wing C.; Piwnski, John J.; McCormick, Kevin D.

PATENT ASSIGNEE(S): Schering Corporation, USA  
SOURCE: PCT Int. Appl., 137 pp.  
CODEN: PIXKD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9634864	A1	19961107	WO 1996-US5660	19960501
W:	AL, AM, AU, AZ, BB, BG, BR, BY, CA, CH, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LA, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5719156	A	19980217	US 1995-432739	19950502
CA 2218887	AA	19961107	CA 1996-221887	19960501
AU 9657141	A1	19961121	AU 1996-57141	19960501
AU 705683	B2	19990527		
EP 823906	A1	19980219	EP 1996-915342	19960501
EP 823906	B1	20030709		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
BR 9600245	A	19990504	BR 1996-0245	19960501
JP 11504921	T2	19990511	JP 1996-533555	19960501
AT 244712	E	20030715	AT 1996-915342	19960501
ES 2197230	T3	20040101	ES 1996-915342	19960501
CA 2228370	AA	19970306	CA 1996-2228370	19960829
CA 2228370	C	20021001		
WO 9708166	A1	19970306	WO 1996-1B1018	19960829
W:	AL, AM, AU, AZ, BB, BG, BR, BY, CA, CH, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LA, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9669979	A1	19970319	AU 1996-69979	19960829
AU 708834	B2	19990812		
EP 850236	A1	19980701	EP 1996-931188	19960829
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			



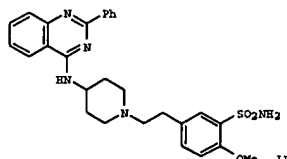
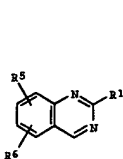
L7 ANSWER 39 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1996:56769 CAPLUS  
DOCUMENT NUMBER: 125:221856  
TITLE:

Preparation of quinazoline derivatives as adrenergic  $\alpha_1C$  receptor antagonists  
INVENTOR(S): Andrews, Robert Carl; Brown, Peter Jonathan; Deaton, David Norman; Drewry, David Harold; Foley, Michael Andrew; Garrison, Deanna T.; Marron, Brian Edward; Shalley, Terrence L.; Berman, Judd M.; Noble, Stewart Alywyn

PATENT ASSIGNEE(S): Glaxo Inc, USA  
SOURCE: Brit. UK Pat. Appl., 190 pp.  
CODEN: BAKXDU

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2295387	A1	19960529	GB 1994-23635	19941123
PRIORITY APPL. INFO.:			GB 1994-23635	19941123
OTHER SOURCE(S):			MARPAT 125:221856	
GI				

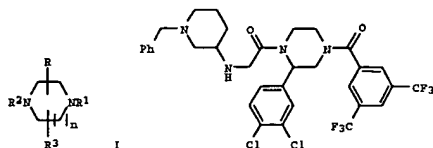


AB Title compds. [I; R = Z1Z2 = R4; R1 = H, halo, alkyl, alkoxy, etc.; R4 = H, (di)(alkyl)amino, phenyl(oxy), etc.; R5, R6 = H, OH, halo, alkyl, alkoxy; Z1 = NH, 2-(piperazine-1,4-diyl)ethylimino, iminopyridine-5,2-dylimino, etc.; Z2 = bond, (un)substituted alkylene] were prepared as adrenergic  $\alpha_1C$  receptor antagonists (no data). Thus, 4-chloro-2-phenylquinazoline was aminated by 4-amino-1-benzylpiperidine and the deprotected product N-alkylated by 5-(2-chloroethyl)-2-methoxybenzenesulfonamide (preparation given) to give title compound II.  
IT 5271-26-1, 2-Phenylpiperazine  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of quinazoline derivs. as adrenergic  $\alpha_1C$  receptor antagonists)

BN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

LT, LV, FI			
JP 10511105	T2	19981027	JP 1997-510069
JP 3447745	B2	20030914	19960829
CN 1200120	A	19981125	CN 1996-197720
CN 1111529	B	20030618	19960829
BR 9610277	A	19990706	BR 1996-10277
JP 2000344766	A2	20001212	JP 2000-153870
JP 3315970	B2	20002019	19960829
IL 123112	A1	20010430	IL 1996-123112
AT 202776	E	20010715	AT 1996-931188
ES 2150345	T3	20010901	ES 1996-931188
US 5892039	A	19990406	US 1996-706016
ZA 9701467	A	19970820	ZA 1997-1467
BR 9705028	A	19971230	19970220
NO 215672	B1	20011103	NO 1997-5028
NO 9800848	A	19980430	NO 1998-848
HK 1005092	A1	20031128	HK 1998-104240
US 5981520	A	19991109	US 1998-99221
GR 3036675	T3	20011231	GR 2001-401532
PRIORITY APPL. INFO.:			US 1995-432739
			A 19950502
			US 1995-50849
			P 19950831
			WO 1996-US5660
			A 19960501
			US 1996-663880
			A 19960614
			JP 1997-510069
			A3 19960829
			WO 1996-1B1018
			W 19960829

OTHER SOURCE(S): MARPAT 126:59974  
GI



AB Title compds. [I; R = H, (hydroxy)alkyl, alkoxyalkyl, aminoalkyl, etc.; R1 = C(=O)(CH2)4R5; R2 = C(=O)N(CH2)R6; R3 = (CH2)uR7; R4 = (hydroxy)alkyl, alkoxyalkyl, phenylalkyl, etc.; R5, R6 = (hetero)aryl; R6 = substituted NH2, N-attached heterocyclyl, etc.; K = O, S, (alkyl)imino, H2; 1,n,u = 0-2; m = 1 and y = 1-3 or m = 2 and y = 0] were prepared. Thus, 2-(3,4-dichlorophenyl)piperazine (preparation given) was aminated by 3,5-(F3C)2C6H3COCl and the product successively condensed with BrCH2COBr and 4-amino-1-benzylpiperidine to give title compound II. Data for in vitro biol. activity of I were given.  
IT 5271-26-1F, 2-Phenylpiperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 1-benzoyl-2-[(4-piperidinylamino)acetyl]piperazines and analogs as neurokinin antagonists)

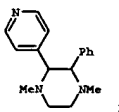
BN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 40 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1996:145361 CAPLUS  
DOCUMENT NUMBER: 124:274756  
TITLE:

Photoinduced Charge Separation Promoted by Ring Opening of a Piperazine Radical Cation  
AUTHOR(S): Lucia, Lucian A.; Whitten, David G.; Schanze, Kirk S.  
CORPORATE SOURCE: Department of Chemistry, University of Florida, Gainesville, FL 32611, USA  
SOURCE: Journal of the American Chemical Society (1996), 118(12), 3057-8  
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI

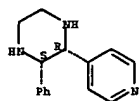


AB The photochem. and photophysics of (bpy)ReI(CO)3(cis-pip)+ and (bpy)ReI(CO)3(trans-pip)+ (c-1 and t-1, resp.) were examined (bpy = 2,2'-bipyridine; cis- and trans-pip = cis- and trans-1, resp.). Steady state irradiation of c-1 produces t-1 with high quantum efficiency. The c-1  $\rightarrow$  t-1 photoisomerization proceeds via (1) a Re  $\rightarrow$  bpy metal-to-ligand charge-transfer excited state (MLCT), (2) a charge-separated state where bpy is reduced and piperazine is oxidized, and (3) a charge-separated state where the piperazine cation radical exists as a ring-opened distonic radical cation formed by fragmentation of the 2,3-ML bond. Nanosecond laser flash photolysis of c-1 reveals two absorbing transients: the first is assigned to the MLCT state while the second is attributed to the second charge-separated state. The decay kinetics of the latter are considerably slower than typically observed for charge-separated states in metal complex dyads. This unusual feature is attributed to the fact that this charge-separated state cannot decay directly to t-1 by charge recombination, but rather decays via a pathway involving a high-energy diradical intermediate.

IT 175405-83-1F 175405-85-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(for preparation of dimethyl(phenyl)pyridylpiperazines)

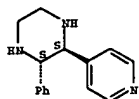
BN 175405-83-1 CAPLUS  
CN Piperazine, 2-phenyl-3-(4-pyridinyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



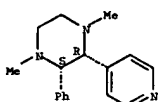
RN 175405-85-3 CAPLUS  
CN Piperazine, 2-phenyl-3-(4-pyridinyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



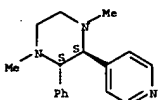
IT 175405-84-2P 175405-85-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(for preparation of rhodium carbonyl bipyridine dimethyl(phenyl)pyridylpiperazine complex)  
RN 175405-84-2 CAPLUS  
CN Piperazine, 1,4-dimethyl-2-phenyl-3-(4-pyridinyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



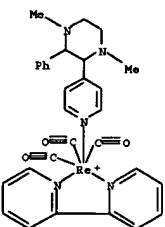
RN 175405-86-4 CAPLUS  
CN Piperazine, 1,4-dimethyl-2-phenyl-3-(4-pyridinyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

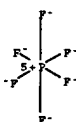


IT 175405-81-9P  
RL: FRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and photoinduced charge separation promoted by ring opening of a

OMP C30 H29 NS O3 Re  
CCI CCS

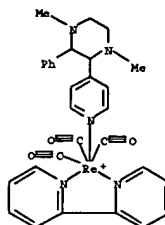


OM 2  
CRN 16919-18-9  
OMP F6 P  
CCI CCS

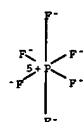


L7 ANSWER 41 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1995:629823 CAPLUS  
DOCUMENT NUMBER: 123:313927  
TITLE: Synthesis of Nitrogen-Containing Macrocycles with Reductive Intramolecular Coupling of Aromatic Diamines  
AUTHOR(S): Kise, Naoki; Oike, Hideaki; Okazaki, Eiichi; Yoshimoto, Masami; Shono, Tatsuya  
CORPORATE SOURCE: Graduate School of Engineering, Kyoto University, Sakyo, 606-01, Japan  
SOURCE: Journal of Organic Chemistry (1995), 60(13), 3980-92  
CODEN: JOCEAH; ISSN: 0022-3263  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 123:313927  
AB Reductive intramol. coupling of aromatic diamines is an effective method for the synthesis of a variety of nitrogen-containing macrocycles. Thus, 1,4-diasacrow ethers were synthesized by intramol. coupling of bis(imino ethers) promoted by electroredn. or chemical reduction with zinc powder in the presence of methanesulfonic acid. In spite of the formation of macrocycles, the yields of 1,4-diasacrow ethers were relatively high.

piperazine radical cation)  
RN 175405-81-9 CAPLUS  
CN Rhodium(1+), (2,2'-bipyridine-N,N')tricarboxyl[1,4-dimethyl-2-phenyl-3-(4-pyridinyl)piperazine-N3]-, [OC-6-33-(cis)]-, hexafluorophosphate(1-) (9CI) (CA INDEX NAME)  
OM 1  
CRN 175405-80-8  
OMP C30 H29 NS O3 Re  
CCI CCS



OM 2  
CRN 16919-18-9  
OMP F6 P  
CCI CCS



IT 175521-04-7P  
RL: FRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and photoinduced charge separation promoted by ring opening of a piperazine radical cation)  
RN 175521-04-7 CAPLUS  
CN Rhodium(1+), (2,2'-bipyridine-N,N')tricarboxyl[1,4-dimethyl-2-phenyl-3-(4-pyridinyl)piperazine-N3]-, [OC-6-33-(trans)]-, hexafluorophosphate(1-) (9CI) (CA INDEX NAME)

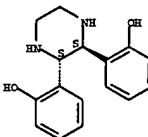
OM 1  
CRN 175521-03-6

This was explained by the formation of proton-bridged intermediates in which intramol. hydrogen bonds are formed between hydrogen and oxygen atoms of diimino salts. Method B was more effective in the formation of 1,4-diasacrow-12-crown-4 deriva. 3 (n = 1) due to the template effect of Zn2+. Optically active macrocyclic bis(lactones) were synthesized stereoselectively by reductive intramol. coupling of bis(imino esters) with zinc powder. The high stereoselectivity is explained by considering a proton-bridged intermediate. The resultant compds. 4 were transformed to optically active 1,2-diarylethylenediamines 7. Various sizes of macrocyclic bis(lactams) were synthesized by reductive intramol. coupling of bis(imino amides) with zinc powder. Reduction of 5 gave the corresponding macrocyclic polyamines 6.  
IT 81602-00-8P 169395-32-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of macrocyclic compds. via reductive coupling of aromatic diamines)  
RN 81602-00-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

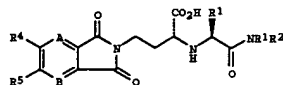


RN 169395-32-8 CAPLUS  
CN Phenol, 2,2'-(2,3-piperazinediyl)bis-, trans- (9CI) (CA INDEX NAME)  
Relative stereochemistry.



L7 ANSWER 42 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1995:460473 CAPLUS  
DOCUMENT NUMBER: 122:240435  
TITLE: Preparation of aminobutanoic acid compounds having metalloprotease inhibiting properties  
INVENTOR(S): McElroy, Andrew R.; Brown, Peter J.; Drewry, David H.; Selovich, James M.; Schoonen, Frank J.  
PATENT ASSIGNEE(S): Glaxo, Inc., USA  
SOURCE: U.S., 33 pp. Cont.-in-part of U.S. Ser. No. 905,934, abandoned.  
CODEN: USYKAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
 US 5326760 A 19940705 US 1993-31439 19930315  
 WO 9400119 A1 19940106 WO 1993-056212 19930628  
 W: AT, AU, BE, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LA, LU, MD, MG, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, CA, CN, ML, MR, NE, SN, TD, TO  
 AU 9346578 A1 19940124 AU 1993-46578 19930628  
 PRIORITY APPL. INFO.: AU 1992-905934 B2 19920629  
 US 1993-31439 A 19930315  
 WO 1993-056212 A 19930628  
 OTHER SOURCE(S): MARPAT 122:240435  
 GI



AB Title compds. I; A, B = N, CR, R = H, halo, alkyl, alkoxy; R1 = alkyl, alkylthioalkyl, R2 = H, alkyl, hydroxyalkyl; R3 = alkyl, alkoxy, alkylamino, (substituted) aryl, arylsulfonyl, etc.; NR2R3 = (substituted) heterocyclyl, R4 = H, CH, alkyl, alkoxy, halo; R5 = H, alkyl, amino, aminoalkyl, acetylamino, (substituted) aryl, arylsulfonylamino, NO2, alkylsulfonylamino, OH, alkoxy, halo, morpholino, piperazinyl, piperidinyl, etc.; R4R5 = atoms to form a (substituted) (aromatic) (heterocyclic) ring, were prepared as metalloprotease inhibitors (no data). Thus, N-[(R)-1-[(1,1-dimethylethoxy)carbonyl]-3-(1,3-dihydro-1,3-dioxo-2H-benz[f]isindol-2-yl)propyl]leucine (preparation given), 2-morpholin-4-ylethylamine, diisopropylethylamine, dihydrobenzotriazole, and benzotriazolyltetramethyluronium hexafluorophosphate were stirred in DMF at 0-20° to give 4-(1,3-dihydro-1,3-dioxo-2H-benz[f]isindol-2-yl)-2(R)-[(3-methyl-1-(S)-[(2-morpholin-4-ylethyl)amino]carbonyl)butyl]amino]butanoic acid 1,1-dimethylethyl ester. This was kept in CF3COOH/BD to give 4-(1,3-dihydro-1,3-dioxo-2H-benz[f]isindol-2-yl)-2(R)-[(3-methyl-1-(S)-[(2-morpholin-4-ylethyl)amino]carbonyl)butyl]amino]butanoic acid.  
 IT 5368-28-5, 3-Oxo-2-phenylpiperazine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, in preparation of aminobutanoate derivative metalloprotease inhibitor)  
 RN 5368-28-5 CAPLUS  
 CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



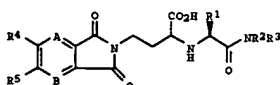
L7 ANSWER 43 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
 ACCESSION NUMBER: 1995:374734 CAPLUS  
 DOCUMENT NUMBER: 122:160683  
 TITLE: Preparation of piperazinylquinolinecarboxylic acids as



● 2 HCl

L7 ANSWER 44 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
 ACCESSION NUMBER: 1994:681234 CAPLUS  
 DOCUMENT NUMBER: 121:281234  
 TITLE: Aminobutanoic acid compounds having metalloprotease inhibiting properties  
 INVENTOR(S): McElroy, Andrew B.; Brown, Peter J.; Drewry, David H.; Salovich, James M.; Schoenen, Frank J.  
 PATENT ASSIGNER(S): Glaxo Inc., USA  
 SOURCE: PCT Int. Appl., 114 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

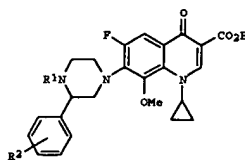
PATENT NO. KIND DATE APPLICATION NO. DATE  
 WO 9400119 A1 19940106 WO 1993-056212 19930628  
 W: AT, AU, BE, BG, BR, CA, CH, CE, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LA, LU, MD, MG, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, CA, CN, ML, MR, NE, SN, TD, TO  
 US 5326760 A 19940705 US 1993-31439 19930315  
 AU 9346578 A1 19940124 AU 1993-46578 19930628  
 PRIORITY APPL. INFO.: AU 1992-905934 A 19920629  
 US 1993-31439 A 19930315  
 WO 1993-056212 A 19930628  
 OTHER SOURCE(S): MARPAT 121:281234  
 GI



AB Aminobutanoic acids of formula I (R1-R5 = substituents), novel intermediates, a pharmaceutical composition for treating inflammatory diseases, demyelinating diseases, and tumor metastasis, methods for such treatment and processes for preparing compds. of formula I. I are matrix metalloprotease inhibitors and as such are useful in the prevention of conditions which involve tissue breakdown, such as rheumatoid arthritis.  
 IT 5368-28-5, 3-Oxo-2-phenylpiperazine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant for α-(amino)-ε-phthalimidobutanoic acid matrix

bactericides  
 INVENTOR(S): Ito, Yasuo; Kato, Hideo; Yasuda, Shingo; Kato, Moryuki; Yoshida, Toohiko; Suzuki, Tomio; Yamamoto, Yoichi  
 PATENT ASSIGNER(S): Hokuriku Pharmaceutical, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.  
 CODEN: JKKKAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
 JP 06271568 A2 19940927 JP 1993-85123 19930322  
 PRIORITY APPL. INFO.: JP 1993-85123 19930322  
 OTHER SOURCE(S): MARPAT 122:160683  
 GI



AB The title compds. I (R1 = H, alkyl, etc.; R2 = H, alkoxy, etc.), useful as bactericides (no data), are prepared I (R1 = R2 = H) was prepared in a 2-step process.  
 IT 5271-26-1, 2-Phenylpiperazine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of piperazinylquinolinecarboxylic acids as bactericides)  
 RN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT 161115-88-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of piperazinylquinolinecarboxylic acids as bactericides)  
 RN 161115-88-4 CAPLUS  
 CN Piperazine, 2-(2-methylphenyl)-, dihydrochloride (9CI) (CA INDEX NAME)

metalloprotease inhibitor)  
 RN 5368-28-5 CAPLUS  
 CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 45 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
 ACCESSION NUMBER: 1994:579620 CAPLUS  
 DOCUMENT NUMBER: 121:179620  
 TITLE: quinolone and naphthyridinecarboxylic acids  
 INVENTOR(S): Bartel, Stephan; Kleefeld, Gerd; Schulze, Thomas; Peessens, Arnold; Neumann, Rainer; Reesfischlaeger, Juergen; Streissle, Gert  
 SOURCE: Bayer A.-G., Germany  
 Ger. Offen., 76 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

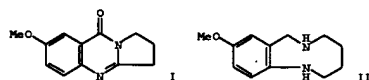
PATENT NO. KIND DATE APPLICATION NO. DATE  
 DE 4303657 A1 19940811 DE 1993-4303657 19930209  
 AU 9453148 A1 19940811 AU 1994-53148 19940112  
 AU 670470 B2 19960718  
 EP 612731 A1 19940831  
 EP 612731 B1 19970820  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, AT 157088 E 19970915 AT 1994-101223 19940127  
 ES 2105362 T3 19971016 ES 1994-101223 19940127  
 AA 2115021 CA 1994-2115021 19940204  
 JP 06271570 A2 19940927 JP 1994-32000 19940204  
 ZA 9400841 A ZA 1994-841 19940209  
 HU 70044 A2 19950928 HU 1994-352 19940208  
 PRIORITY APPL. INFO.: DE 1993-4303657 A 19930209  
 OTHER SOURCE(S): MARPAT 121:179620  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. I (R1 = H, hydroxy, halo, etc.; R2 = H, nitro, halo; R3 = piperazinyl; R4 = aminoalkyl; R5 = H, halo, alkyl, etc.; R6 = hydroxy, benzoyloxy, alkoxy, morpholino, etc.; D = H, amino, alkyl, etc.; A = methine, nitrogen) were disclosed. I are useful as virucides. An example compound, the [(3-methoxyphenyl)piperazinyl]quinolinecarboxylic acid II, was prepared II inhibited HIV in vitro in infected cells (IC50 = 3 μM).  
 IT 5271-26-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant for (piperazinyl)quinolinecarboxylate)  
 RN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 46 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1994:269233 CAPLUS  
 DOCUMENT NUMBER: 120:269233  
 TITLE: Sodium borohydride-boron trifluoride etherate, a convenient and efficient reagent for the reduction of amides  
 AUTHOR(S): Sengupta, Sreela; Sahn, Devi P.; Chatterjee, Sunil K.  
 CORPORATE SOURCE: Div. Chem. Technol., Central Drug Res. Inst., Lucknow, 226 001, India  
 SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1994), 32B(3), 285-7  
 CODEN: IJSEBD, ISSN: 0376-4699  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 120:269233  
 GI



AB Sodium borohydride-boron trifluoride etherate has been employed as a reducing agent for the conversion of amides into amines, the reducing species being diborane generated in situ. This method successfully reduces primary, secondary and tertiary amides, lactams and chiral diketopiperazines, in moderate to high yields. An unusual ring cleavage is observed in the reduction of the pyrrolo[2,1-b]quinazolin-1-one (I) resulting in the formation of benzo-1,6-diazine (II).  
 IT 5271-26-1P Piperazine, 2-phenyl-  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 EN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

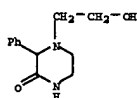


L7 ANSWER 47 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:587608 CAPLUS  
 DOCUMENT NUMBER: 119:107608  
 TITLE: A composition and method for simultaneous absorption

FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5167941	A	19921201	US 1990-623313	19901206
US 5019365	A	19910528	US 1990-546075	19900629
			US 1988-277159	B2 19881120
			US 1990-546075	A2 19900629

 PRIORITY APPL. INFO.:  
 OTHER SOURCE(S): MARPAT 119:102416  
 AB SO2-oxidation is inhibited in alkaline scrubbing solns. for removal of SO2 from flue gases by adding 1-3000 ppm of a polyelectrolyte containing quaternary ammonium groups (mol. weight >10,000) to the scrubbing solution. The scrubbing solution contains amines, e.g., piperazines, morpholines, piperidines, piperazines, piperazinediones, hydantoins, triazinones, pyrimidines, oxazolidones, and N-carboxymethyl ethylenediamines. Suitable polyelectrolytes include the reaction products of starch and chlorohydroxypropyl tri-Me ammonium salt or glycidyl tri-Me ammonium chloride, poly(diallyldimethylammonium chloride) and copolymers of acrylamide and quaternary ammonium compts.  
 IT 23936-08-5  
 RL: USES (Uses)  
 (sulfur dioxide scrubbing solns. containing, and antioxidants for sulfites)  
 EN 23936-08-5 CAPLUS  
 CN Piperazine, 4-(2-hydroxyethyl)-3-phenyl- (9CI) (CA INDEX NAME)

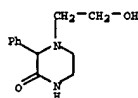


L7 ANSWER 49 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:448767 CAPLUS  
 DOCUMENT NUMBER: 119:48767  
 TITLE: Stereochemistry of 1,3,4-trimethyl-2-phenylpiperazines: divergence between calculated NMR and NMR determination of proportions of conformational equilibrium  
 AUTHOR(S): Gelboke, M.; Tytgat, D.  
 CORPORATE SOURCE: Lab. Chim. Pharm. Org., Univ. Libre de Bruxelles, Bruxelles, B-1050, Belg.  
 SOURCE: Bulletin des Societes Chimiques Belges (1993), 102(1), 67-74  
 CODEN: BSCBAG, ISSN: 0037-9646  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 AB Cis- and trans-1,3,4-trimethyl-2-phenylpiperazine have been synthesized and their most stable conformers were estimated by the MMX88.9 program. In the cis derivative at room temperature a rapid equilibrium between two conformers differing in the stereochem. of the atoms at the position 2 and 3 was predicted (ratio = 7:3). The major species would be the conformer with an axial Ph. Their IR- and 13C-NMR spectra taken at different temps. confirm the existence of such an equilibrium in the cis compts. but a discrepancy in their proportion is noticed. The major species has an equatorial Ph.  
 IT 148502-22-1P 148502-23-2F 148518-39-2P

INVENTOR(S): of sulfur dioxide and nitric oxide  
 Chang, Dane; Bedell, Stephen A.; Kirby, Larry H.  
 PATENT ASSIGNEE(S): Dow Chemical Co., USA  
 SOURCE: PCT Int. Appl., 47 pp.  
 CODEN: PIKMD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9303825	A1	19930304	WO 1992-US6736	19920812
W: CA, DE, GB, JP				
EW: AT, BE, CH, DE, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
CA 2093901	AA	19930214	CA 1992-2093901	19920812
EP 552360	A1	19930728	EP 1992-918433	19920812
R: DE, GB				
JP 06502349	T2	19940317	JP 1993-504406	19920812
GB 2264488	A1	19930901	GB 1993-7576	19930413
GB 2264488	B2	19950222		
PRIORITY APPL. INFO.:			US 1991-744157	A 19910813
			WO 1992-US6736	W 19920812

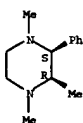
OTHER SOURCE(S): MARPAT 119:107608  
 AB SO2 and NO are simultaneously removed from flue gases by an absorption process and apparatus using an absorbent composition comprising an aqueous solution of chelates and sulfite salt for NO abatement and amine SO2 absorbents such as piperazines, morpholines, piperidines, piperazines, piperazinediones, hydantoins, triazinones, pyrimidines, oxazolidones, etc., for SO2 abatement. SO2 is thermally stripped from the spent absorbent and recovered. Metal chelates oxidized to an inactive state as a side-reaction are electrochem. reduced. An anionic exchange membrane in the electrochem. cell regenerates heat stable amine salt byproducts to be converted back to usable amine sorbent, and facilitates removal from the absorbent solution of other waste salts.  
 IT 23936-08-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 EN 23936-08-5 CAPLUS  
 CN Piperazine, 4-(2-hydroxyethyl)-3-phenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 48 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:502416 CAPLUS  
 DOCUMENT NUMBER: 119:102416  
 TITLE: Quaternary polyamines as sulfite oxidation inhibitors in amine scrubbing of sulfur dioxide  
 INVENTOR(S): Bedell, Stephen A.  
 PATENT ASSIGNEE(S): Dow Chemical Co., USA  
 SOURCE: U.S., 12 pp. Cont.-in-part of U.S. 5,019,365.  
 CODEN: USYKAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

148518-40-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and conformational equilibrium of)  
 EN 148502-22-1 CAPLUS  
 CN Piperazine, 1,2,4-trimethyl-3-phenyl-, dihydrochloride, cis- (9CI) (CA INDEX NAME)

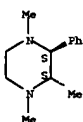
Relative stereochemistry.



●2 HCl

EN 148502-23-2 CAPLUS  
 CN Piperazine, 1,2,4-trimethyl-3-phenyl-, dihydrochloride, trans- (9CI) (CA INDEX NAME)

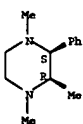
Relative stereochemistry.



●2 HCl

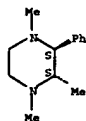
EN 148518-39-2 CAPLUS  
 CN Piperazine, 1,2,4-trimethyl-3-phenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



EN 148518-40-5 CAPLUS  
 CN Piperazine, 1,2,4-trimethyl-3-phenyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L7 ANSWER 50 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1993:125768 CAPLUS  
DOCUMENT NUMBER: 118:125768  
TITLE: Air-activatable polymerizable compositions  
INVENTOR(S): Eneaney, Brendan; Guthrie, John; Melody, David P.  
PATENT ASSIGNER(S): Locitite (Ireland) Ltd., Ire.  
SOURCE: Eur. Pat. Appl., 31 pp.  
CODEN: EPXKDW

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 502733	A1	19920909	EP 1992-301899	19920305
EP 502733	B1	19970910		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
CA 2062400	AA	19920907	CA 1992-2062400	19920305
NO 3200871	A	19920907	NO 1992-871	19920305
NO 300693	B1	19970707		
AU 9211439	A1	19920910	AU 1992-11439	19920305
AU 646148	B2	19940210		
BR 9200743	A	19921110	BR 1992-743	19920305
AT 157993	E	19970916	AT 1992-301899	19920305
ES 2106824	T3	19971116	ES 1992-301899	19920305
JP 05105846	A2	19930427	JP 1992-84533	19920306
JP 2952103	B2	19990920		

PRIORITY APPL. INFO.:

AB Peroxide-free title compds. which cure in the presence or absence of air, useful for 1-package adhesives and coatings, contain 21 free-radically polymerizable monomer and 21 auto-oxidizable compound such as imines having the N not bonded to another N and compds. containing C:CN groups with the C:CN not part of a Ph ring as polymerization catalyst. The compds. may contain soluble salts as catalysts and weak organic acids to control the oxidation rate of the auto-oxidizable compds. Thus, a composition containing hydroxypropyl methacrylate, acrylic acid, Co naphthenate, Me methacrylate, hydrocarbon oil, and 3,5-diethyl-N-phenyl-2-propyl-1,2-dihydropyridine was applied to a steel plate exposed to air for 1 min, and the coated plate was pressed onto a similarly coated steel plate 1.5 min at 3 kg load to give a laminate with tensile shear bond strength 14.6 N/cm<sup>2</sup>.

IT 146362-58-5

RL: CAT (Catalyst use); USES (Uses)  
(catalysts, air-activatable, for polymerization of free-radically polymerizable monomers as adhesives or coatings)

RN 146362-58-5 CAPLUS

benzodiazepines II and/or 5-acetyl-2-methyl-10-substituted 2,3,4,5,6,7-hexahydro-1H-2,5-benzodiazepines III (Sommelet-Hauser rearrangement products). However, a similar treatment of 1-methyl-3-oxo-2-phenyl-1-trimethylsilylmethylpiperazinium iodide (IV) afforded 1-methyl-6-phenyl-2,3,6,7-tetrahydro-1H-diazepine-5-one (V) (Stevens rearrangement product).

IT 145729-99-3P 145730-00-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and Stevens rearrangement of)

RN 145729-99-3 CAPLUS

CN Piperazinium, 1-methyl-3-oxo-2-phenyl-1-[(trimethylsilyl)methyl]-, iodide, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

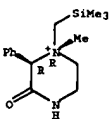


● I-

RN 145730-00-3 CAPLUS

CN Piperazinium, 1-methyl-3-oxo-2-phenyl-1-[(trimethylsilyl)methyl]-, iodide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● I-

IT 145729-86-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and acetylation of)

RN 145729-86-8 CAPLUS

CN Piperazine, 2-phenyl-1-[(trimethylsilyl)methyl]- (9CI) (CA INDEX NAME)

CN Pyrazine, tetrahydro-2,3-diphenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

CM 1

CRN 146362-57-4

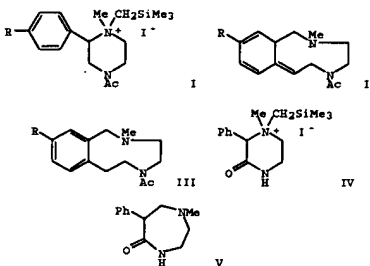
CMF C23 H24 N2



L7 ANSWER 51 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1993:80918 CAPLUS  
DOCUMENT NUMBER: 118:80918

TITLE: Sommelet-Hauser or Stevens rearrangement of 1-methyl-2-(substituted phenyl)piperazinium 1-methylides. Ring enlargement of piperazines to seven- or nine-membered cyclic amines  
AUTHOR(S): Kitano, Tomoko; Shirai, Machiro; Motoi, Manami; Sato, Yoshiro  
CORPORATE SOURCE: Fac. Pharm. Sci., Nagoya City Univ., Nagoya, 467, Japan  
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (21), 2851-4  
CODEN: JOCPEB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 118:80918  
GI



AB Fluoride ion-induced desilylation of 4-acetyl-1-methyl-2-(4-substituted phenyl)-1-trimethylsilylmethylpiperazinium iodides I (R = H, MeO) gave 5-acetyl-2-methyl-10-substituted 1,3,4,5,6,11a-hexahydro-2H-2,5-

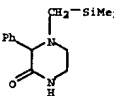


IT 145729-84-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and reduction or methylation-quaternization of)

RN 145729-84-6 CAPLUS

CN Piperazinone, 3-phenyl-4-[(trimethylsilyl)methyl]- (9CI) (CA INDEX NAME)



IT 5368-28-5, 3-Phenyl-2-piperazinone

RL: RCT (Reactant); RACT (Reactant or reagent)  
(silylation of)

RN 5368-28-5 CAPLUS

CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 52 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:625747 CAPLUS

DOCUMENT NUMBER: 117:225747

TITLE: Effects of 3,3'-N,N'-trimethyl-2-phenyl-1,4-piperazine diastereomers on monoamine uptake and monoamine oxidase in rat brain  
AUTHOR(S): Smith, D. P.; Jensen, P. N.; Gelbock, M.; Tytgat, D.  
CORPORATE SOURCE: Psychopharmacol. Res. Unit, Psychiatr. Hosp., Risakov, Den.

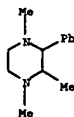
SOURCE: Journal of Neural Transmission: General Section (1992), 88(3), 177-85  
CODEN: JNGSE9; ISSN: 0300-9564

DOCUMENT TYPE: Journal

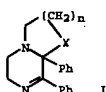
LANGUAGE: English

AB The diastereomers of 3,3'-N,N'-trimethyl-2-phenyl-1,4-piperazine dihydrochloride (TPP) were tested for their effects on NA, DA and 5-HT uptake in synaptosomes prepared from hypothalamus, corpus striatum, and frontal cortex, resp. The diastereomers differed with respect to their inhibitory properties. (2R, 3R)-TPP was more potent than the other diastereomers on NA and DA uptake, whereas (2S, 3S)-TPP was least potent. In contrast, the (2S, 3S)- and (2S, 3R)-diastereomers of TPP were more potent than (2R, 3R)- and (2R, 2S)-TPP as inhibitors of 5-HT uptake. None of the diastereomers affected monoamine oxidase activity. The findings

show that the diastereomers of TPP interact stereoselectively with neuronal mechanisms for monoamine uptake, and that the (S)-configuration of the 2 carbon is important for inhibitory actions of TPP on 5-HT uptake.  
IT 115238-12-5D, diastereomers  
RL: BIOL (Biological study)  
(monoamine uptake and monoamine oxidase in brain response to)  
RN 115238-12-5 CAPLUS  
CN Piperazine, 1,2,4-trimethyl-3-phenyl- (9CI) (CA INDEX NAME)

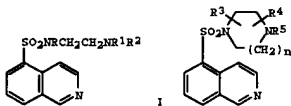


L7 ANSWER 53 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1992:591810 CAPLUS  
DOCUMENT NUMBER: 117:191810  
TITLE: Preparation and hydrogenolysis of fused piperazines by reaction of diamine and triamine derivatives with benzil. Application to the synthesis of terminal N-monoprotected triamines  
AUTHOR(S): Okawara, Tadaaki; Uchiyama, Koichi; Okamoto, Yoshinari; Yamasaki, Tetsuo; Furukawa, Mitsuru  
CORPORATE SOURCE: Pac. Pharma. Sci., Kumamoto Univ., Kumamoto, 862, Japan  
SOURCE: Journal of Chemical Research, Synopses (1992), (8), 244-5  
CODEN: JRPSCD; ISSN: 0308-2342  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 117:191810  
OI



AB Reaction of diamine and triamine derive. with benzils affords tetrahydrooxazolo-pyrazines hexahydroimidazolo-pyrazines and hexahydro-pyrazine-pyrimidines I (X = O, NH; n = 1, 2). Their application to the synthesis of terminal N-monooxylated triamines, e.g., R2N(CH2)2NH(CH2)2NHR2 is described.  
IT 143699-18-7P 143699-19-8F 143699-20-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and benzylation of)  
RN 143699-18-7 CAPLUS  
CN 1-Piperazineethanol, 2,3-diphenyl- (9CI) (CA INDEX NAME)

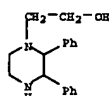
LANGUAGE: English  
OI



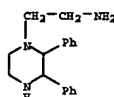
AB On the basis of a hypothesis that cyclization and alkylation of the diamine part of aminoalkylisoquinolinesulfonamides, e.g., I (R,R1,R2 = H, alkyl), would give highly active compounds, a new series of 5-isoquinolinesulfonamide derivs., II (R3 = H, 2-, 3-Me; R4 = H, 3-, 5-Me; R5 = H, alkyl, aryl, acyl, n = 1,2) were prepared from cyclic diamines. Their vasodilating effects were subsequently evaluated in vivo according to the increase in arterial blood flow after injection locally into the femoral and/or vertebral arteries of dogs. Cyclization of the diamine structure in I gave very potent vasodilators. II (R3-R5 = H; n = 1 (III), 2 (IV)). Acylation and sulfonylation of the terminal amino nitrogen afforded much less potent compounds. In contrast to the hypothesis, alkylation on the ring carbon and the terminal nitrogen of the cyclic amine afforded less active compounds, except for II (R3 = 2-Me, R4 = 5-Me, R5 = H, n = 2) (V). The most active compounds, III IV and V showed more potent vasodilating effects and more selective activity in the vertebral artery than either teripidil or diltiazem.  
IT 5271-26-1, 2-Phenylpiperazine  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(sulfonylation of, with isoquinolinesulfonyl chloride)  
RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 55 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1992:83485 CAPLUS  
DOCUMENT NUMBER: 116:83485  
TITLE: Generation of 2-azaallyl anions by the transmetalation of N-(trialkylstannyl)methanimines. Pyrrolidine synthesis by [3 + 2] cycloadditions with alkenes  
AUTHOR(S): Pearson, William H.; Sauer, Daniel P.; Poetsch, Michael J.  
CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA  
SOURCE: Journal of the American Chemical Society (1992), 114(4), 1329-45  
CODEN: JACSAT; ISSN: 0002-7863  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 116:83485  
OI



RN 143699-19-8 CAPLUS  
CN 1-Piperazineethanamine, 2,3-diphenyl- (9CI) (CA INDEX NAME)



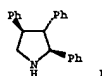
RN 143699-20-1 CAPLUS  
CN 1-Piperazinepropanamine, 2,3-diphenyl- (9CI) (CA INDEX NAME)



IT 143699-24-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 143699-24-5 CAPLUS  
CN Piperazine, 2,3-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 54 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1992:255586 CAPLUS  
DOCUMENT NUMBER: 116:255586  
TITLE: 5-Isoquinolinesulfonamide derivatives. III. Synthesis and vasodilatory activity of 1-(5-isoquinolinesulfonyl)piperazine derivatives  
AUTHOR(S): Morikawa, Anri; Soma, Takanori; Asano, Toshio  
CORPORATE SOURCE: Life-Sci. Inst., Asahi Chem. Ind. Co., Ltd., Nobeoka, 882, Japan  
SOURCE: Chemical & Pharmaceutical Bulletin (1992), 40(3), 770-3  
CODEN: CPBTLA; ISSN: 0009-2363  
DOCUMENT TYPE: Journal



AB Treatment of N-(trimethylstannyl)methanimines or N-(tributylstannyl)methanimines with MeLi or BuLi, resp., affords 2-azaallyl anions by tin-lithium exchange. These anions undergo intramol. or intermol. [x1s + x2s] cycloaddns. with alkenes and alkynes to generate pyrrolidines or pyrrolines after quenching with water or other electrophiles. Thus, treatment of (azaallyl)stannane PhCH2NCH2SnMe3 with MeLi, then trans-stilbene afforded pyrrolidine I in 83% yield after work-up. The tin-lithium exchange method allows unstabilized 2-azaallyl anions to be generated for the first time. The lifetime of the anions is limited by a competing intramol. side reaction. Therefore, relatively reactive alkenes and alkynes must be used, such as stilbene, styrenes, enynes, diphenylacetylene, vinyl sulfides, vinyl selenides, and vinylsilanes. The latter three types of anionophiles afford functionalized cycloadducts which may be transformed into more useful pyrrolidines by reduction, elimination, or oxidation. A synthesis of the alkaloid

(a)-mesembrane was accomplished using an intramol. 2-azaallyl anion cycloaddn.  
IT 81602-00-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 81602-00-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

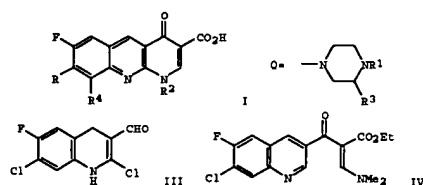
Relative stereochemistry.



L7 ANSWER 56 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1992:6538 CAPLUS  
DOCUMENT NUMBER: 116:6538  
TITLE: Preparation of 8-piperazinobenzo[b][1,6]naphthyridin-4-one-3-carboxylates as antibacterial and antiviral agents  
INVENTOR(S): Antoine, Michel; Barreau, Michel; Desconclois, Jean  
PATENT ASSIGNER(S): Francois, Girard, Philippe; Picaut, Guy  
SOURCE: Laboratoire Roger Ballou S. A., Fr.  
Dnr. Pat. Appl., 38 pp.  
CODEN: EPYKDW  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 431991	A1	19910612	EP 1990-403047	19901029
EP 431991	B1	19940112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2653643	A1	19910503	FR 1989-14203	19891030
FR 2653643	B1	19920110		
FR 2664595	A1	19920117	FR 1990-8757	19900710
FR 2664595	B1	19920918		
RO 108347	B1	19940420	RO 1990-146144	19901022
CA 2028730	AA	19910501	CA 1990-2028730	19901029
AU 8065551	A1	19910502	AU 1990-65551	19901029
AU 629997	B2	19921015		
NO 9004683	A	19910502	NO 1990-44683	19901029
NO 175433	B	19940704		
NO 175433	C	19941012		
HU 55778	A2	19910628	HU 1990-6926	19901029
HU 208138	B	19930830		
ZA 9008639	A	19910828	ZA 1990-8639	19901029
AT 100103	E	19940115	AT 1990-403047	19901029
FI 92068	B	19940615	FI 1990-5329	19901029
FI 92068	C	19940926		
PL 164270	B1	19940729	PL 1990-287543	19901029
ES 2062455	T3	19941216	ES 1990-403047	19901029
IL 96159	A1	19941229	IL 1990-96159	19901029
CZ 280513	B6	19940214	CZ 1990-5297	19901029
JP 03151384	A2	19910627	JP 1990-293501	19901030
US 5053509	A	19911001	US 1990-605340	19901030
HU 2047613	C1	19951110	HU 1992-5011989	19920708
PRIORITY APPLN. INFO.:				
			FR 1989-14203	A 19891030
			FR 1990-8757	A 19900710
			EP 1990-403047	A 19901029

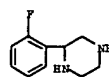
OTHER SOURCE(S): MARPAT 116:6538  
G1



AB Title compds. [I; R = piperazine group O; R1 = H, CH<sub>3</sub>, alkyl; R2 = H, (fluoro)alkyl, cycloalkyl, alkoxyl, alkylamino; R3 = (un)substituted Ph, phenylalkyl, etc.; R4 = H, F] (II) were prepared. Thus, ClCH<sub>2</sub>CH<sub>2</sub>COCl was condensed with 3,4-difluoro-6-chloro-2,3-dihydroquinoline which, under Vilsmeier-Haack conditions, gave dihydroquinoline III. The latter was converted in 4 steps to quinolinylpiperazine IV which was cyclized with MeNH<sub>2</sub> to give, after saponification, I (R = Cl, R2 = Me, R4 = H) (V). Condensation of V with 2-phenylpiperazine gave II (R1 = R4 = H, R2 = Me, R3 = Ph). I are active against *Staphylococcus aureus* IP 8203 in mice at 4-150 mg/kg orally.

IT 137684-18-5P 137766-74-6F 137766-76-8P

RL: RCT (Reactant), SPN (Synthetic preparation), PREP (Preparation), RACT (Reactant or reagent)  
(preparation and reaction of, in preparation of bactericides and antiviral agents)  
EN 137684-18-5 CAPLUS  
CN Piperazine, 2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



EN 137766-74-6 CAPLUS  
CN Piperazine, 2-phenyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



EN 137766-76-8 CAPLUS  
CN Piperazine, 2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 5271-26-1  
RL: RCT (Reactant), RACT (Reactant or reagent)  
(reaction of, in preparation of bactericides and antiviral agents)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 57 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1991:613993 CAPLUS  
DOCUMENT NUMBER: 115:213993  
TITLE: Quaternary polyamines as sulfite oxidation inhibitors in scrubbers  
INVENTOR(S): Bedell, Stephen A.  
PATENT ASSIGNEE(S): Dow Chemical Co., USA  
SOURCE: U.S., 5 pp. Cont.-in-part of U.S. Ser. No. 277,159, abandoned.

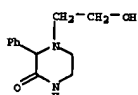
DOCUMENT TYPE: CODEN: USYKAM  
LANGUAGE: Patent  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION: English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5019365	A	19910528	US 1990-546075	19900629
BR 8906214	A	19900626	BR 1989-6214	19891127
CA 2004051	AA	19900529	CA 1989-2004051	19891128
DK 8906001	A	19900530	DK 1989-6001	19891128
NO 8904741	A	19900530	NO 1989-4741	19891128
AU 8945671	A1	19900607	AU 1989-45671	19891128
CN 1043088	A	19900620	CN 1989-109553	19891128
CN 1033005	B	19961016		
JP 02194815	A2	19900801	JP 1989-306759	19891128
ZA 8909106	A	19910731	ZA 1989-9106	19891129
US 5167941	A	19921201	US 1990-623313	19901206
PRIORITY APPLN. INFO.:				
			US 1988-277159	B2 19881129
			US 1990-546075	A2 19900629

OTHER SOURCE(S): MARPAT 115:213993

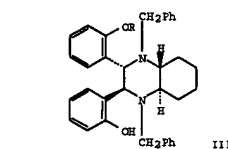
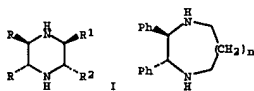
AB SO<sub>2</sub>-oxidation is inhibited in alkaline scrubbing solns. for removal of SO<sub>2</sub> from gases by adding 1-3000 ppm of a polyelectrolyte containing quaternary ammonium groups (mol. weight >10,000) to the scrubbing solution which also contains 20-1M piperazine or morpholine compds. Suitable polyelectrolytes are poly(diallyldimethylammonium chloride) and N-(3-chloro-2-hydroxypropyl)pyridinium chloride.

IT 23936-08-5  
RL: USES (Uses)  
(sulfur dioxide scrubbing solns. containing, and antioxidants for sulfites)  
EN 23936-08-5 CAPLUS  
CN Piperazine, 4-(2-hydroxyethyl)-3-phenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 58 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1991:247236 CAPLUS  
DOCUMENT NUMBER: 114:247236

TITLE: Electroorganic chemistry. 129. Electrocatalytic synthesis of chiral piperazines and enantioselective addition of diethylzinc to aldehydes in the presence of the chiral piperazines  
AUTHOR(S): Shono, Tatsuaki; Kise, Naoki; Shirakawa, Eiji; Matsumoto, Hideshi; Okazaki, Eiichi  
CORPORATE SOURCE: Fac. Eng., Kyoto Univ., Kyoto, 606, Japan  
SOURCE: Journal of Organic Chemistry (1991), 56(9), 3063-7  
CODEN: JOCEAH; ISSN: 0022-3263  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 114:247236  
G1



AB Electroredn. of chiral diimines RCH=NCH(R1)CH(R2)N=CHR [R = Ph, 4-MeOC<sub>6</sub>H<sub>4</sub>, 4-ClC<sub>6</sub>H<sub>4</sub>, 1-naphthyl; R1 = H, Me, Me<sub>2</sub>CHCH<sub>2</sub>; R2 = H; R1R2 = (CH<sub>2</sub>)<sub>4</sub>] in acidic media gave intramol. coupled products, 2,3-diaryl piperazines I, stereoselectively. Seven- and eight-membered cyclic compds. II (n = 1, 2) were synthesized by the same method. Benzylated piperazines III (R = H, CH<sub>2</sub>Ph) were effective chiral ligands of catalysts for the enantioselective addition of diethylzinc to aldehydes. Thus, adding Et<sub>2</sub>Zn to PhCHO in the presence of III (R = H) gave (S)-1-phenylpropanol.

IT 81602-00-8F 169395-32-8P  
RL: SPN (Synthetic preparation), PREP (Preparation)  
(preparation of)

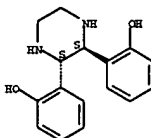
EN 81602-00-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

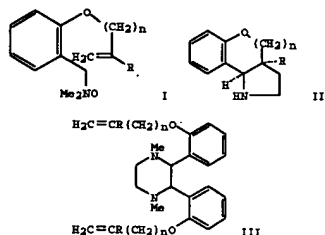


EN 169395-32-8 CAPLUS  
CN Phenol, 2,2'-(2,3-piperazinediyl)bis-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

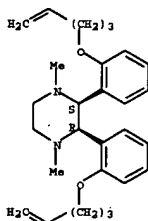


L7 ANSWER 59 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1991:42733 CAPLUS  
 DOCUMENT NUMBER: 114:42733  
 TITLE: The [3+2] intramolecular cycloaddition reaction of  
 azomethine ylides generated from benzylic N-oxides  
 Roussi, Georges  
 CORPORATE SOURCE: Inst. Chim. Subst. Nat., CNRS, Gif-sur-Yvette, 91190,  
 Fr.  
 SOURCE: Heterocycles (1990), 31(8), 1445-50  
 CODEN: HETCYM; ISSN: 0385-5414  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 114:42733  
 GI



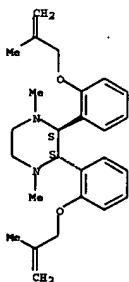
AB Intramol. cycloaddn. of azomethine ylides, generated from benzylic  
 N-oxides I (n = 1, 2, 3; R = H, Me), give tricyclic compds. II (n = 1, 2;  
 R = H, Me) and cis- and trans-piperazines III (R = Me, n = 1, R = H, n =  
 2, 3) upon reaction with LDA.  
 IT 131471-15-3F 131471-18-6F 131471-20-0P  
 131471-21-1P 131471-23-3F 131471-24-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 131471-15-3 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-bis[2-[(2-methyl-2-propenyl)oxy]phenyl]-,  
 cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



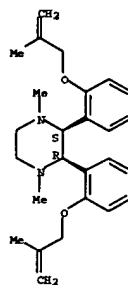
RN 131471-21-1 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-bis[2-[(2-methyl-2-propenyl)oxy]phenyl]-,  
 trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



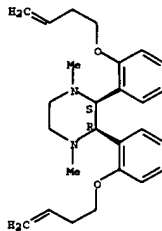
RN 131471-23-3 CAPLUS  
 CN Piperazine, 2,3-bis[2-(3-butenyloxy)phenyl]-1,4-dimethyl-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



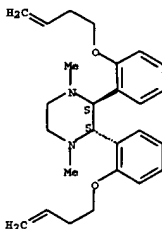
RN 131471-16-6 CAPLUS  
 CN Piperazine, 2,3-bis[2-(3-butenyloxy)phenyl]-1,4-dimethyl-, cis- (9CI) (CA  
 INDEX NAME)

Relative stereochemistry.



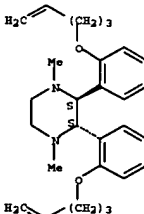
RN 131471-20-0 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-bis[2-(4-pentenyl)oxy]phenyl]-, cis- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



RN 131471-24-4 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-bis[2-(4-pentenyl)oxy]phenyl]-, trans- (9CI)  
 (CA INDEX NAME)

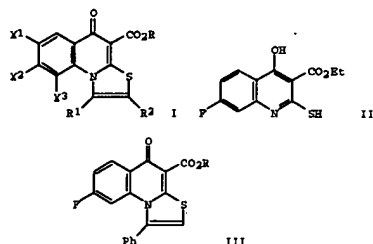
Relative stereochemistry.



L7 ANSWER 60 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1990:406328 CAPLUS  
 DOCUMENT NUMBER: 113:6328  
 TITLE: Preparation of thiasoloquinolonecarboxylic acid  
 derivatives and their pharmaceutical compositions as  
 antitumor agents  
 INVENTOR(S): Hosomi, Jiro; Asahina, Yoshikazu; Suzue, Seigo  
 PATENT ASSIGNER(S): Kyorin Pharmaceutical Co., Ltd., Japan; Kyowa Hakko  
 Kogyo Co., Ltd.  
 SOURCE: PCT Int. Appl., 61 pp.  
 CODEN: PINKD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8912055	A1	19891214	WO 1989-JP581	19890607

W: KR, US  
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE  
JP 02138284 A2 19900528 JP 1989-142545 19890605  
PRIORITY APPLN. INFO.: JP 1988-139396 A 19880608  
JP 1988-199229 A 19880812  
OTHER SOURCE(S): MARPAT 113:6328  
GI



AB The title compds. [I; R = H, C2-6 alkyl; R1, R2 = H, C1-6 alkyl, (fluoro)phenyl, X1, X3 = H, F; X2 = halo, (substituted) pyrrolidine, piperazine, etc.; dotted line denotes single or double bond], useful as antitumor agents and DNA topoisomerase II inhibitors, are prepared. Refluxing a mixture of 2.24 mmol mercaptan compound II and 2.46 mmol PhCOCH2Et in EtOH, concentration, filtration of the residue in Et2O-EtOH suspension, stirring the resulting crystals in CP3803H, adding H2O, and extraction with CHCl3 gave 70 mg ester III (R = Et) and 260 mg acid III (R = H). Also prepared were 35 addnl. I which showed IC50 of 0.18-0.31 µg/mL against human colon cancer DLD-1 cells, vs. 0.82 µg/mL with etoposide. A tablet formulation was given.  
IT 5271-26-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, in preparation of antitumor agents)  
RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 61 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1990:216960 CAPLUS  
DOCUMENT NUMBER: 112:216960  
TITLE: Thienylpiperazines, their preparation and use as  
nootropics  
INVENTOR(S): Schoenafinger, Karl; Beyerle, Rudi; Schindler, Ursula  
PATENT ASSIGNEE(S): Cassella A.-G., Fed. Rep. Ger.

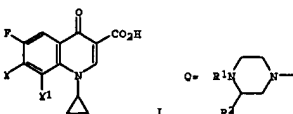


● HCl

L7 ANSWER 62 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1990:178712 CAPLUS  
DOCUMENT NUMBER: 112:178712  
TITLE: Preparation and formulation of 1-cyclopropyl-6,7-difluoro-1,4-dehydro-4-oxo-3-quinoline carboxylic acid and analogs  
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.  
SOURCE: Can., 31 pp. Division of Can. Appl. No. 482,912.  
CODEN: CAXX44  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1259315	A2	19890912	CA 1988-577424	19880914
DE 3420770	A1	19851205	DE 1984-3420770	19840604
CA 1248954	A1	19890117	CA 1985-482912	19850531
			DE 1984-3420770	19840604
			CA 1985-482912	19850531
			DE 1984-3420798	19840604

PRIORITY APPLN. INFO.:  
OTHER SOURCE(S): MARPAT 112:178712  
GI

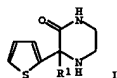


AB Title compds. I (X = Cl, F, O; X1 = H, F; R1 = H, (un)substituted C1-4 alkyl; R2 = (un)substituted cyclohexyl, -Ph) their hydrates or salts are useful as antibacterials against gram-pos. and -neg. organisms, and as preservatives for inorg. and organic materials (no data) are prepared I (X = Cl, X1 = H), OH (R1 = H, R2 = Ph), and 1,4-diazabicyclo[2.2.2]octane in DMSO were heated at 140° for 4 h to give 32% I (X = 3-phenyl-1-piperazinyl, X1 = H) (II). In test against Klebsiella the MIC was 0.015 µg/mL vs. 1 µg/mL for norfloxacin. A pharmaceutical formulation comprising I is given.  
IT 5271-26-1, 2-Phenylpiperazine  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(substitution by, of quinolinecarboxylate derivative)  
RN 5271-26-1 CAPLUS

SOURCE: Eur. Pat. Appl., 13 pp.  
CODEN: EPYXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 342536	A1	19891123	EP 1989-108550	19890512
EP 342536	B1	19920923		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8903766	A	19900228	ZA 1989-3766	19880519
DE 3817198	A1	19891130	DE 1988-3817198	19880520
DE 8902145	A	19891121	DE 1989-2145	19890502
US 4898866	A	19900206	US 1989-349540	19890509
AT 80885	E	19921015	AT 1989-108550	19890512
ES 2052807	T3	19940716	ES 1989-108550	19890512
JP 02017185	A2	19900122	JP 1989-124583	19890519
HU 55388	A2	19910528	HU 1989-2509	19890519
			DE 1988-3817198	19880520
			EP 1989-108550	19890512

PRIORITY APPLN. INFO.:  
OTHER SOURCE(S): CASREACT 112:216960; MARPAT 112:216960  
GI



AB The title compds. [I; R1 = (substituted) Ph, phenylalkyl, naphthylalkyl, alkoxyalkyl, aminoalkyl] were prepared. Thus, MeMgI in Et2O was added at room temperature to 3-(2-thienyl)-5,6-dihydropyrazine-2-one in THF. The mixture was stirred 15 h to give I (R1 = Me). I at 30 mg/kg orally in mice gave 24-49% reversal of NaNO2-induced cerebral hypoxia.  
IT 127044-86-4F 127044-92-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as nootropic)  
RN 127044-86-4 CAPLUS  
CN Piperazine, 3-phenyl-3-(2-thienyl)- (9CI) (CA INDEX NAME)



RN 127044-92-2 CAPLUS  
CN Piperazine, 3-phenyl-3-(2-thienyl)-, monohydrochloride (9CI) (CA INDEX NAME)

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

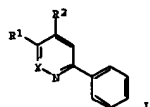


L7 ANSWER 63 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1989:619301 CAPLUS  
DOCUMENT NUMBER: 111:219301  
TITLE: Pyridine or pyridazine derivatives as cardioprotective agents and for the treatment of ischemic disease, and process for their preparation  
INVENTOR(S): Takaya, Takao; Takasugi, Hisashi; Esumi, Kinio; Kuno, Atsushi; Sakai, Hiroyoshi; Maeda, Kazuhiro; Sakamoto, Yoshie  
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan  
SOURCE: Eur. Pat. Appl., 13 pp.  
CODEN: EPYXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 311322	A2	19890412	EP 1988-309155	19881003
EP 311322	A3	19901122		
EP 311322	B1	19930721		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4857527	A	19890915	US 1988-184195	19880421
ZA 8806889	A	19890530	ZA 1988-6889	19880915
FI 8804418	A	19890406	FI 1988-4418	19880927
AU 8823338	A1	19890601	AU 1988-23338	19881003
AU 621067	B2	19920305		
JP 01207234	A2	19890821	JP 1988-249593	19881003
AT 91626	E	19930815	AT 1988-309155	19881003
ES 2058301	T3	19941101	ES 1988-309155	19881003
DK 8805549	A	19890406	DK 1988-5549	19881004
NO 8804399	A	19890406	NO 1988-4399	19881004
CN 1041569	A	19900425	CN 1988-109132	19881004
HU 51614	A2	19900528	HU 1988-5132	19881004
CA 1317296	A1	19930504	CA 1988-579295	19881004
US 4990507	A	19910205	US 1989-294742	19890109

PRIORITY APPLN. INFO.:  
OTHER SOURCE(S): MARPAT 111:219301  
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 1987-251771	A	19871005		
US 1988-184195	A	19880421		
GB 1985-30602	A	19851212		
US 1986-940923	A2	19861212		
JP 1987-145996	A	19870611		
ZA 1988-6889	A	19880915		
EP 1988-309155	A	19881003		

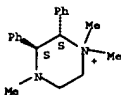


AB Pharmaceuticals contain, as a cardioprotective agent or a therapeutic agent for ischemic disease, a phenylpyridine or phenylpyrazine derivative I (R1 = alkyl substituted by a heterocyclic group; carbonyl substituted by heterocyclic(lower)alkyl or alkylamino(lower)alkyl; N-containing heterocyclic carbonyl which is optionally substituted by lower alkyl, or ureido substituted by lower alkylamino(lower)alkyl; (a) R2 = nitrophenyl; X = -N, -CH3; R3 = lower alkyl; (b) R2 = lower alkyl; X = -CH3; R3 = nitrophenyl), salts of I, and carriers and excipients. A solution containing N-(aminooethyl)morpholine (170.5 g) in Me isobutyl ketone (200 mL) was added to a solution of diketene (102 mL) in Me isobutyl ketone (1.3 L) at -10° to -10° and to the resulting solution which contained N-(2-morpholinoethyl)acetacetamide was added 3-(3-nitrophenyl)-1-phenyl-2-propen-1-one (220.4 g) and AcONH4 (100 g) and the mixture was stirred at 80° for 4.5 h to give 1,4-dihydro-3-(2-morpholinoethylcarbonyl)-2-methyl-4-(3-nitrophenyl)-6-phenylpyridine. The latter compound was oxidized with MnO2 (700 g) to give 3-(2-morpholinoethylcarbonyl)-2-methyl-4-(3-nitrophenyl)-6-phenylpyridine (II) (154 g; 39.6% yield). Isolated guinea pig hearts were perfused with a medium containing 10 + 10-6 g/mL II and ischemia was induced by stopping the perfusion. The change in cardiac depression (i.e. left ventricular systolic pressure + heart rate) was +4.1%, compared to a control; the recovery of ATP content of the heart was 96.3%; and the coronary flow was decreased by 1.6%. Tablets containing 2 mg II each were manufactured from a mixture containing II (100 g),

hydroxypropyl Me cellulose (500 g), lactose (6.87 kg), low-substituted hydroxypropyl cellulose (1.5 kg), and Mg stearate (30 g).  
IT 5271-26-1D, 2-phenylpiperazine, derivs.  
RL: BIOL (Biological study)  
(as cardioprotective agents and agents for treatment of ischemic disease)  
RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



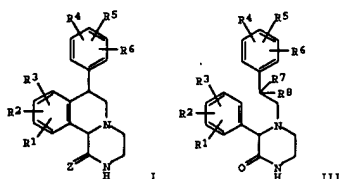
L7 ANSWER 64 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
ACCESSION NUMBER: 1989:553759 CAPLUS  
DOCUMENT NUMBER: 111:153759  
TITLE: Scope of the reductive coupling of aromatic aldimines using low-valent titanium reagents to form 1,2-diarylethylendiamines  
AUTHOR(S): Betschart, Claudia; Schmidt, Beat; Seebach, Dieter  
CORPORATE SOURCE: Lab. Org. Chem., Eidg. Tech. Hochschule, Zurich, CH-8092, Switz.  
SOURCE: Helvetica Chimica Acta (1988), 71(8), 1999-2021  
CODEN: HCACAV, ISSN: 0018-019X



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L7 ANSWER 65 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
ACCESSION NUMBER: 1989:497285 CAPLUS  
DOCUMENT NUMBER: 111:97285  
TITLE: A process for preparation of cis-1,3,4,6,7,11b-hexahydro-7-aryl-2H-pyrazino[2,1-a]isoquinoline derivatives as drugs  
PATENT ASSIGNER(S): Penwalt Corp., USA  
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.  
CODEN: JKKXAP  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01031772	A2	19890202	JP 1987-182418	19870723
PRIORITY APPLN. INFO.:			JP 1987-182418	19870723
OTHER SOURCE(S):		MARPAT 111:97285		



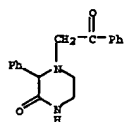
AB The title compds. [I; Z = H2; R1-R6 sep. = H, halo, OH, NH2, lower aminoalkyl, CF3, lower alkyl, lower alkoxy, lower di- or monoalkylamino] (II), useful as drugs, e.g. antidepressants, were prepared from 3-phenyl-4-phenacyl-2-piperazine derivs. (III; R7R8 = O). Reduction of 3-phenyl-4-(4-chlorophenacyl)-2-piperazine (preparation given) with NaBH4 in MeOH at ≤50° to 3-phenyl-4-(2-hydroxy-2-(4-chlorophenyl)ethyl)-2-piperazine and cyclization of the latter alc. by treatment with concentrated H2SO4 gave 98% a 4:5:1 mixture of trans- and cis-I (Z = O, R1-R5 = H, R6 = 4-Cl) (V). Refluxing the latter isomeric mixture in MeOH containing MeONa gave 89% cis-V containing <1% trans-V which was reduced with

DOCUMENT TYPE: Journal  
LANGUAGE: German  
OTHER SOURCE(S): CASREACT 111:153759  
CI

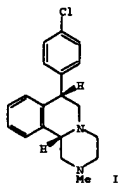


AB 4-RC6H4CH(NMe2)2 and 4-RC6H4CH(NMe2)Cl- (R = H, Me, OMe, Br) were reductively coupled by TiCl4-Mg in THF to give 4-RC6H4CH(NMe2)CH(NMe2)C6H4R-4 with moderate diastereoselectivity. 4-RC6H4CH(NMe2)CH(NMe2)C6H4R-4 similarly gave 4-RC6H4CH(NMe2)CH(NMe2)C6H4R-4. R1R2C(R3)C(R4)C(R5)C(R6)C(R7)C(R8)C(R9)C(R10)C(R11)C(R12)C(R13)C(R14)C(R15)C(R16)C(R17)C(R18)C(R19)C(R20)C(R21)C(R22)C(R23)C(R24)C(R25)C(R26)C(R27)C(R28)C(R29)C(R30)C(R31)C(R32)C(R33)C(R34)C(R35)C(R36)C(R37)C(R38)C(R39)C(R40)C(R41)C(R42)C(R43)C(R44)C(R45)C(R46)C(R47)C(R48)C(R49)C(R50)C(R51)C(R52)C(R53)C(R54)C(R55)C(R56)C(R57)C(R58)C(R59)C(R60)C(R61)C(R62)C(R63)C(R64)C(R65)C(R66)C(R67)C(R68)C(R69)C(R70)C(R71)C(R72)C(R73)C(R74)C(R75)C(R76)C(R77)C(R78)C(R79)C(R80)C(R81)C(R82)C(R83)C(R84)C(R85)C(R86)C(R87)C(R88)C(R89)C(R90)C(R91)C(R92)C(R93)C(R94)C(R95)C(R96)C(R97)C(R98)C(R99)C(R100)C(R101)C(R102)C(R103)C(R104)C(R105)C(R106)C(R107)C(R108)C(R109)C(R110)C(R111)C(R112)C(R113)C(R114)C(R115)C(R116)C(R117)C(R118)C(R119)C(R120)C(R121)C(R122)C(R123)C(R124)C(R125)C(R126)C(R127)C(R128)C(R129)C(R130)C(R131)C(R132)C(R133)C(R134)C(R135)C(R136)C(R137)C(R138)C(R139)C(R140)C(R141)C(R142)C(R143)C(R144)C(R145)C(R146)C(R147)C(R148)C(R149)C(R150)C(R151)C(R152)C(R153)C(R154)C(R155)C(R156)C(R157)C(R158)C(R159)C(R160)C(R161)C(R162)C(R163)C(R164)C(R165)C(R166)C(R167)C(R168)C(R169)C(R170)C(R171)C(R172)C(R173)C(R174)C(R175)C(R176)C(R177)C(R178)C(R179)C(R180)C(R181)C(R182)C(R183)C(R184)C(R185)C(R186)C(R187)C(R188)C(R189)C(R190)C(R191)C(R192)C(R193)C(R194)C(R195)C(R196)C(R197)C(R198)C(R199)C(R200)C(R201)C(R202)C(R203)C(R204)C(R205)C(R206)C(R207)C(R208)C(R209)C(R210)C(R211)C(R212)C(R213)C(R214)C(R215)C(R216)C(R217)C(R218)C(R219)C(R220)C(R221)C(R222)C(R223)C(R224)C(R225)C(R226)C(R227)C(R228)C(R229)C(R230)C(R231)C(R232)C(R233)C(R234)C(R235)C(R236)C(R237)C(R238)C(R239)C(R240)C(R241)C(R242)C(R243)C(R244)C(R245)C(R246)C(R247)C(R248)C(R249)C(R250)C(R251)C(R252)C(R253)C(R254)C(R255)C(R256)C(R257)C(R258)C(R259)C(R260)C(R261)C(R262)C(R263)C(R264)C(R265)C(R266)C(R267)C(R268)C(R269)C(R270)C(R271)C(R272)C(R273)C(R274)C(R275)C(R276)C(R277)C(R278)C(R279)C(R280)C(R281)C(R282)C(R283)C(R284)C(R285)C(R286)C(R287)C(R288)C(R289)C(R290)C(R291)C(R292)C(R293)C(R294)C(R295)C(R296)C(R297)C(R298)C(R299)C(R300)C(R301)C(R302)C(R303)C(R304)C(R305)C(R306)C(R307)C(R308)C(R309)C(R310)C(R311)C(R312)C(R313)C(R314)C(R315)C(R316)C(R317)C(R318)C(R319)C(R320)C(R321)C(R322)C(R323)C(R324)C(R325)C(R326)C(R327)C(R328)C(R329)C(R330)C(R331)C(R332)C(R333)C(R334)C(R335)C(R336)C(R337)C(R338)C(R339)C(R340)C(R341)C(R342)C(R343)C(R344)C(R345)C(R346)C(R347)C(R348)C(R349)C(R350)C(R351)C(R352)C(R353)C(R354)C(R355)C(R356)C(R357)C(R358)C(R359)C(R360)C(R361)C(R362)C(R363)C(R364)C(R365)C(R366)C(R367)C(R368)C(R369)C(R370)C(R371)C(R372)C(R373)C(R374)C(R375)C(R376)C(R377)C(R378)C(R379)C(R380)C(R381)C(R382)C(R383)C(R384)C(R385)C(R386)C(R387)C(R388)C(R389)C(R390)C(R391)C(R392)C(R393)C(R394)C(R395)C(R396)C(R397)C(R398)C(R399)C(R400)C(R401)C(R402)C(R403)C(R404)C(R405)C(R406)C(R407)C(R408)C(R409)C(R410)C(R411)C(R412)C(R413)C(R414)C(R415)C(R416)C(R417)C(R418)C(R419)C(R420)C(R421)C(R422)C(R423)C(R424)C(R425)C(R426)C(R427)C(R428)C(R429)C(R430)C(R431)C(R432)C(R433)C(R434)C(R435)C(R436)C(R437)C(R438)C(R439)C(R440)C(R441)C(R442)C(R443)C(R444)C(R445)C(R446)C(R447)C(R448)C(R449)C(R450)C(R451)C(R452)C(R453)C(R454)C(R455)C(R456)C(R457)C(R458)C(R459)C(R460)C(R461)C(R462)C(R463)C(R464)C(R465)C(R466)C(R467)C(R468)C(R469)C(R470)C(R471)C(R472)C(R473)C(R474)C(R475)C(R476)C(R477)C(R478)C(R479)C(R480)C(R481)C(R482)C(R483)C(R484)C(R485)C(R486)C(R487)C(R488)C(R489)C(R490)C(R491)C(R492)C(R493)C(R494)C(R495)C(R496)C(R497)C(R498)C(R499)C(R500)C(R501)C(R502)C(R503)C(R504)C(R505)C(R506)C(R507)C(R508)C(R509)C(R510)C(R511)C(R512)C(R513)C(R514)C(R515)C(R516)C(R517)C(R518)C(R519)C(R520)C(R521)C(R522)C(R523)C(R524)C(R525)C(R526)C(R527)C(R528)C(R529)C(R530)C(R531)C(R532)C(R533)C(R534)C(R535)C(R536)C(R537)C(R538)C(R539)C(R540)C(R541)C(R542)C(R543)C(R544)C(R545)C(R546)C(R547)C(R548)C(R549)C(R550)C(R551)C(R552)C(R553)C(R554)C(R555)C(R556)C(R557)C(R558)C(R559)C(R560)C(R561)C(R562)C(R563)C(R564)C(R565)C(R566)C(R567)C(R568)C(R569)C(R570)C(R571)C(R572)C(R573)C(R574)C(R575)C(R576)C(R577)C(R578)C(R579)C(R580)C(R581)C(R582)C(R583)C(R584)C(R585)C(R586)C(R587)C(R588)C(R589)C(R590)C(R591)C(R592)C(R593)C(R594)C(R595)C(R596)C(R597)C(R598)C(R599)C(R600)C(R601)C(R602)C(R603)C(R604)C(R605)C(R606)C(R607)C(R608)C(R609)C(R610)C(R611)C(R612)C(R613)C(R614)C(R615)C(R616)C(R617)C(R618)C(R619)C(R620)C(R621)C(R622)C(R623)C(R624)C(R625)C(R626)C(R627)C(R628)C(R629)C(R630)C(R631)C(R632)C(R633)C(R634)C(R635)C(R636)C(R637)C(R638)C(R639)C(R640)C(R641)C(R642)C(R643)C(R644)C(R645)C(R646)C(R647)C(R648)C(R649)C(R650)C(R651)C(R652)C(R653)C(R654)C(R655)C(R656)C(R657)C(R658)C(R659)C(R660)C(R661)C(R662)C(R663)C(R664)C(R665)C(R666)C(R667)C(R668)C(R669)C(R670)C(R671)C(R672)C(R673)C(R674)C(R675)C(R676)C(R677)C(R678)C(R679)C(R680)C(R681)C(R682)C(R683)C(R684)C(R685)C(R686)C(R687)C(R688)C(R689)C(R690)C(R691)C(R692)C(R693)C(R694)C(R695)C(R696)C(R697)C(R698)C(R699)C(R700)C(R701)C(R702)C(R703)C(R704)C(R705)C(R706)C(R707)C(R708)C(R709)C(R710)C(R711)C(R712)C(R713)C(R714)C(R715)C(R716)C(R717)C(R718)C(R719)C(R720)C(R721)C(R722)C(R723)C(R724)C(R725)C(R726)C(R727)C(R728)C(R729)C(R730)C(R7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CN Piperazinone, 4-(2-oxo-2-phenylethyl)-3-phenyl- (9CI) (CA INDEX NAME)

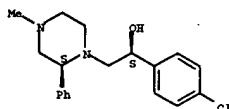


L7 ANSWER 66 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1989:477964 CAPLUS  
DOCUMENT NUMBER: 111:77964  
TITLE: New atypical antidepressants: an efficient process for preparing cis-1,3,4,6,7,11b-hexahydro-2-methyl-7-aryl-2H-pyrazino[2,1-a]isoquinolines  
AUTHOR(S): Schmiesing, Richard J.; Matz, James R.  
CORPORATE SOURCE: Phara. Div., Pennwalt Corp., Rochester, NY, 14603, USA  
SOURCE: Heterocycles (1989), 29(2), 359-63  
CODEN: HETCYM, ISSN: 0365-5414  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 111:77964  
CI



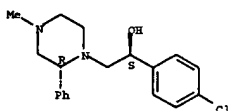
AB Pyrazinoisoquinoline derivative I was prepared by a multistep procedure starting from 3-phenyl-2-piperazinone.  
IT 118654-13-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
EN 118654-15-2 CAPLUS  
CN Piperazine, 1-methyl-3-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



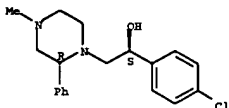
RN 121851-78-3 CAPLUS  
CN 1-Piperazineethanol,  $\alpha$ -(4-chlorophenyl)-4-methyl-2-phenyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 121851-79-4 CAPLUS  
CN 1-Piperazineethanol,  $\alpha$ -(4-chlorophenyl)-4-methyl-2-phenyl-, dihydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 2 HCl

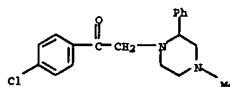
RN 121851-80-7 CAPLUS  
CN 1-Piperazineethanol,  $\alpha$ -(4-chlorophenyl)-4-methyl-2-phenyl-, dihydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

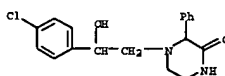


● 2 HCl

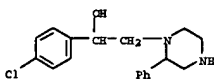
IT 118654-16-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
EN 118654-16-3 CAPLUS  
CN 1-Piperazineethanol,  $\alpha$ -(4-chlorophenyl)-2-(4-methyl-2-phenyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



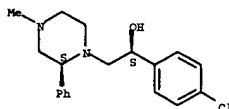
IT 121851-69-2F 121851-72-7F 121851-77-2P  
121851-78-3F 121851-79-4F 121851-80-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
EN 121851-69-2 CAPLUS  
CN Piperazinone, 4-[2-(4-chlorophenyl)-2-hydroxyethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 121851-72-7 CAPLUS  
CN 1-Piperazineethanol,  $\alpha$ -(4-chlorophenyl)-2-phenyl- (9CI) (CA INDEX NAME)

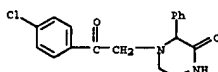


RN 121851-77-2 CAPLUS  
CN 1-Piperazineethanol,  $\alpha$ -(4-chlorophenyl)-4-methyl-2-phenyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)



● 2 HCl

IT 118654-13-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
EN 118654-13-0 CAPLUS  
CN Piperazinone, 4-[2-(4-chlorophenyl)-2-oxoethyl]-3-phenyl- (9CI) (CA INDEX NAME)



IT 5271-26-1F, 2-Phenylpiperazine  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



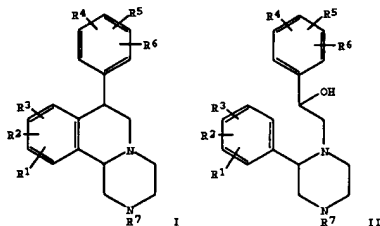
IT 5368-28-5, 3-Phenyl-2-piperazinone  
RL: RCT (Reactant); RACT (Reactant or reagent)  
EN 5368-28-5 CAPLUS  
CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 67 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1989:75567 CAPLUS  
DOCUMENT NUMBER: 110:75567  
TITLE: Processes for the preparation of trans-1,3,4,6,7,11b-

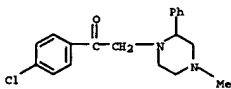
hexahydro-7-aryl-2H-pyrazino[2,1-a]isoquinolines as  
antidepressants, antihistaminics, and cholinergics  
Schmiesing, Richard J.  
PENNALT CORP., USA  
U.S., 9 pp.  
CODEN: USXXAM  
Patent  
English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4772705	A	19880920	US 1985-759022	19850725
EP 300074	A1	19890125	EP 1987-116629	19870722
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
PRIORITY APPL. INFO.:		US 1985-759022		19850725
OTHER SOURCE(S):		CASREACT 110:75567; MARPAT 110:75567		

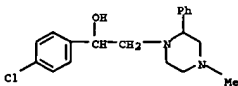


AB The title compds. I (R1-R3 = H, halo, OH, amino, lower aminoalkyl, CF3, etc.; R4-R6 = H, halo, OH, NO2, amino, lower aminoalkyl, etc.; R7 = H, lower alkyl), useful as antidepressants, antihistaminics, and cholinergics (no data) were prepared from phenylpiperazines II. N-Alkylation of 3-phenyl-2-piperazinone (preparation given) with 4-chlorophenacyl bromide, followed by reduction, cyclization in H2SO4, and workup, gave trans-1,3,4,4',7,11b-hexahydro-7-(4-chlorophenyl)-2H-pyrazino[2,1-a]isoquinoline-2HCl.

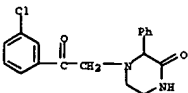
IT 5368-28-5P, 3-Phenyl-2-piperazinone 118654-13-OP  
118654-14-1P 118654-15-2F 118654-16-3P  
118654-17-4P 118654-18-5F 118678-27-6F,  
3-Phenyl-4-phenacyl-2-piperazinone  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, in preparation of antidepressant, antihistaminic, and cholinergic)  
RN 5368-28-5 CAPLUS  
CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



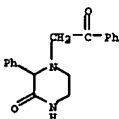
RN 118654-17-4 CAPLUS  
CN 1-Piperazineethanol, alpha-(4-chlorophenyl)-4-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 118654-18-5 CAPLUS  
CN Piperazinone, 4-[2-(2-chlorophenyl)-2-oxoethyl]-3-phenyl- (9CI) (CA INDEX NAME)



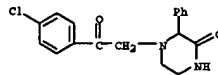
RN 118678-27-6 CAPLUS  
CN Piperazinone, 4-(2-oxo-2-phenylethyl)-3-phenyl- (9CI) (CA INDEX NAME)



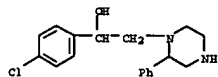
L7 ANSWER 68 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1988:437834 CAPLUS  
DOCUMENT NUMBER: 109:37834  
TITLE: Preparation of phenylpiperazines as antidepressants and sedatives  
INVENTOR(S): Lafon, Louis  
PATENT ASSIGNER(S): Laboratoire L. Lafon, Fr.  
SOURCE: Fr. Demande, 33 pp.  
CODEN: FRXXBL  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1



RN 118654-13-0 CAPLUS  
CN Piperazinone, 4-[2-(4-chlorophenyl)-2-oxoethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 118654-14-1 CAPLUS  
CN 1-Piperazineethanol, alpha-(4-chlorophenyl)-2-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 118654-15-2 CAPLUS  
CN Piperazine, 1-methyl-3-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



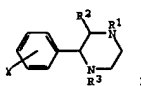
●2 HCl

RN 118654-16-3 CAPLUS  
CN Ethanone, 1-(4-chlorophenyl)-2-(4-methyl-2-phenyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

#### PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2585702	A1	19870206	FR 1985-11684	19850731
FR 2585702	B1	19890303		
EP 211746	A1	19870225	EP 1986-401644	19860723
EP 211746	B1	19900523		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 53026	E	19900615	AT 1986-401644	19860723
DK 8603602	A	19870201	DK 1986-3602	19860729
DK 165876	B	19930201		
DK 165876	C	19930621		
AU 8660691	A1	19870205	AU 1986-60691	19860730
AU 580179	B2	19890105		
ZA 8605685	A	19870325	ZA 1986-5685	19860730
JP 62029576	A2	19870207	JP 1986-181806	19860731
JP 07030047	B4	19950405		
CA 1263392	A1	19891128	CA 1986-515056	19860731
US 4912110	A	19900327	US 1988-283736	19881213
PRIORITY APPL. INFO.:			FR 1985-11684	A 19850731
			EP 1986-401644	A 19860723
			US 1986-891290	B2 19860731

OTHER SOURCE(S): CASREACT 109:37834  
GI



AB The title compds. (I; R1 = H, Cl-4 alkyl; R2 = H, Cl, C2 alkyl; R3 = H, Cl-4 alkyl; X = H, F, Cl, Br) and their salts, useful as antidepressants and sedatives, are prepared. A mixture of PhCOOMe and NH2CH2CH2NH2 (II) in MeOH was allowed to react for 0.5 h and then cooled in an ice bath. MeOH was added, and the reaction mixture was allowed to react overnight to give, after treatment with 3N HCl, 34% I (R1 = R3 = X = H, R2 = Me). 2HCl (III). III and I (R1 = Et, R2 = R3 = H, X = 2-Cl) showed antidepressant and sedative effects in mice in extensive pharmacol. studies.

IT 65709-26-4F 104096-26-6F 115237-99-5P  
115238-03-4F 115238-06-7F 115238-12-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as antidepressant and sedative)

RN 65709-26-4 CAPLUS  
CN Piperazine, 2-(2-chlorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

EN 104096-26-6 CAPLUS  
CN Piperazine, 2-methyl-3-phenyl- (6CI, 9CI) (CA INDEX NAME)

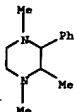


EN 115237-99-5 CAPLUS  
CN Piperazine, 2-methyl-3-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

EN 115238-03-4 CAPLUS  
CN Piperazine, 1,2,4-trimethyl-3-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

EN 115238-06-7 CAPLUS  
CN Piperazine, 2-(2-fluorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

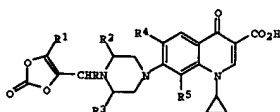
EN 115238-12-5 CAPLUS

IT 5271-26-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with dihydrodibenzocycloheptylideneacetyl chloride)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



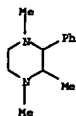
L7 ANSWER 70 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1986:608934 CAPLUS  
DOCUMENT NUMBER: 105:208934  
TITLE: 1-Cyclopropyl-1,4-dihydro-4-oxo-7-[4-(2-oxo-1,3-dioxol-4-ylmethyl)-1-piperazinyl]-3-quinolinecarboxylic acids and their use and formulation as antibacterial agents  
INVENTOR(S): Petersen, Uwe; Grobe, Klaus; Zeiler, Hans Joachim; Metzger, Karl Georg  
PATENT ASSIGNER(S): Bayer A.-G., Fed. Rep. Ger.  
SOURCE: Ger. Offen., 49 pp.  
CODEN: GWXKX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3504643	A1	19860814	DE 1985-3504643	19850212
US 4703047	A	19871027	US 1986-022714	19860127
EP 191390	A1	19860820	EP 1986-101348	19860203
EP 191390	B1	19890823		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 45730	E	19890915	AT 1986-101348	19860203
JP 61186399	A2	19860820	JP 1986-24237	19860207
JP 07080076	B4	19950830		
PRIORIT. APPL. INFO.: DE 1985-3504643 A 19850212				
OTHER SOURCE(S): CASREACT 105:208934				
GI				



AB Title compds. I (R = H, R1 = H, Ph, Cl-4 alkyl, R2 = C2-3 alkylene, R3, R4 = H, Me, Et, (substituted) Ph, cyclohexyl, furyl, tetrahydrofuryl, phenyl, R5 = H, F, Cl, Br, NO2), R5 = H, F, Cl, Br are prepared. These compds. are useful as medical and veterinary bactericides. Thus, I (R = R2 = R3 = R5 = H, R1 = Me, R4 = F) (II) was prepared in 8 steps. II was effective against gram-pos. and gram-neg. bacteria in vitro. I (initial definitions) were formulated as tablets containing 1.583.0, cellulose 55.0,

CN Piperazine, 1,2,4-trimethyl-3-phenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 69 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1987:417884 CAPLUS  
DOCUMENT NUMBER: 107:17884  
TITLE: preparation of novel compounds derived from diphenylmethylethylamine  
INVENTOR(S): Ciera, Xavier D.; Andreoli, Romeo R.; Lloveras, Pedro P.; Braseghini, Leonida; Irujo, Jose P.  
PATENT ASSIGNEE(S): Sociedad Espanola de Especialidades Farmaco-Terapeuticas S. A., Spain  
SOURCE: Span., 62 pp.  
CODEN: SPYKAD  
DOCUMENT TYPE: Patent  
LANGUAGE: Spanish  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 524680	A1	19841216	ES 1983-524680	19830802
EP 132764	A2	19850213	EP 1984-108424	19840717
EP 132764	A3	19851204		
EP 132764	B1	19910102		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
EP 357956	A2	19900314	EP 1989-114293	19840717
EP 357956	A3	19900829		
I: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 59432	E	19910115	AT 1984-108424	19840717
AU 8431316	A1	19850207	AU 1984-31316	19840730
AU 580963	B2	19890209		
ZA 8405940	A	19860827	ZA 1984-5940	19840801
CA 1243018	A1	19881011	CA 1984-460173	19840801
JP 60126265	A2	19850705	JP 1984-163743	19840802
JP 06025091	B4	19940406		
US 4835156	A	19890530	US 1987-54408	19870526
US 4835179	A	19890530	US 1987-54409	19870526
US 5112026	A	19920512	US 1989-336801	19890412
PRIORIT. APPL. INFO.: ES 1983-524680 A 19830802				
EP 1984-108424 P 19840717				
US 1984-635898 A2 19840730				

GI For diagram(s), see printed CA Issue.  
AB The title compds. [I, R1 = H, F, R2 = H, Me, CH2CH2CH2CH2, CH2COCH2CH2COCH2, R3 = H, Me, R4 = H, Ph, 4-ROCH2, X = H2, CH2CH2, CH2CH2, Y = H2, O, Z = CH, (substituted) amino, alkanoyl, alkoxy, or R2Z forms a piperazine ring] are prepared for use as vasodilators, ulcer inhibitors, gastric secretion inhibitors, antispasmodics, antihistaminics, and antidepressants. 10,11-Dihydrodibenzocyclohept-5-ylideneacetic acid was refluxed with SOCl2, and the acid chloride was amidated with 2-phenylpiperazine to yield II in 33% yield. II showed an ED50 of 2.42 + 10-5 M in vitro as a vasodilator in hyperkalemic rats, and an oral ED50 of 32.9 mg/kg as an antitumor agent in indomethacin-treated rats.

corn starch 72.0, polyvinylpyrrolidone 30.0, silica 5.0, Mg stearate 5.0 mg, which were coated with a mixture containing hydroxypropyl Me cellulose 6.0, polyethylene glycol 2.0, and TiO2 2.0 mg.

IT 5271-26-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with fluorinated quinolinecarboxylates)  
EN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



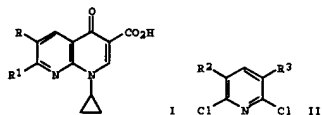
L7 ANSWER 71 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1986:591059 CAPLUS  
DOCUMENT NUMBER: 105:191059  
TITLE: 1-Cyclopropyl-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acids  
INVENTOR(S): Petersen, Uwe; Grobe, Klaus; Zeiler, Hans Joachim; Metzger, Karl Georg  
PATENT ASSIGNER(S): Bayer A.-G., Fed. Rep. Ger.  
SOURCE: Ger. Offen., 64 pp.  
CODEN: GWXKX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3508816	A1	19860710	DE 1985-3508816	19850313
NO 8505134	A	19860711	NO 1985-5134	19851218
NO 163331	B	19900129		
NO 163331	C	19900509		
EP 187376	A2	19860716	EP 1985-116551	19851224
EP 187376	A3	19880594		
EP 187376	B1	19920513		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 74076	E	19920515	AT 1985-116551	19851224
US 4840954	A	19890620	US 1985-815440	19851231
IL 77538	A1	19920525	IL 1986-77538	19860107
FI 8600673	A	19860711	FI 1986-73	19860108
FI 86721	B	19920630		
FI 86721	C	19921012		
DD 241250	A5	19861203	DD 1986-286039	19860108
DD 257427	A5	19880615	DD 1986-296482	19860108
DD 257428	A5	19880615	DD 1986-296483	19860108
CA 1339373	A1	19970826	CA 1986-499241	19860107
DK 860091	A	19860711	DK 1986-91	19860109
DK 148439	B1	19940328		
JP 61161284	A2	19860731	JP 1986-1485	19860109
JP 06053741	B4	19940720		
ZA 8600163	A	19860924	ZA 1986-163	19860109
HU 40126	A2	19861128	HU 1986-87	19860109
HU 193623	B	19871130		
AU 652164	A1	19870122	AU 1986-52164	19860109
AU 574550	B2	19860707		
ES 550767	A1	19880616	ES 1986-550767	19860109
ES 550767	A5	19880715		
PL 140191	B1	19890920	PL 1986-264565	19860109

PL 148759 B1 19891130 PL 1986-257419 19860109  
 HU 202840 B 19910429 HU 1987-1847 19860109  
 CN 86100126 A 19860709 CH 1986-100126 19860110  
 CN 1003239 B 19890208  
 NO 8600199 A 19860711 NO 1986-199 19860121  
 ES 557516 A1 19871016 ES 1987-557516 19870429  
 ES 557515 A1 19880216 ES 1987-557515 19870429  
 ES 557514 A1 19880301 ES 1987-557514 19870429  
 AU 8773118 A1 19870910 AU 1987-73118 19870515  
 AU 576449 B2 19880825  
 ES 557785 A1 19880416 ES 1987-557785 19871215  
 AU 8818359 A1 19880915 AU 1988-18359 19880624  
 FI 8902675 A 19890601 FI 1989-2475 19890601  
 CA 1320206 A2 19930713 CA 1990-415694 19900405  
 DE 1985-350562 A1 19850110  
 DE 1985-350816 A 19850313  
 EP 1985-116551 A 19851224  
 CA 1986-459241 A3 19860108  
 FI 1986-73 A 19860108

PRIORITY APPL. INFO.:  
 CASREACT 105:191059

OTHER SOURCE(S):  
 GI



AB The title compds. [I; R = halo, NO2; R1 = (un)substituted 1-piperazinyl, 1-pyrrolidinyl] were prepared as bactericides and feed additives. Thus, 2,6-dichloro-5-methyl-3-pyridinamine (II, R2 = NH2, R3 = Me) was diazotized and coupled with Me2NH to give II (R2 = Me2NH; R3 = Me) which was fluorinated with HF to give I (R2 = F, R3 = Me). The latter was converted in 4 steps to II (R2 = F, R3 = EtOOC(CH2CH2)CO) which was condensed with cyclopropylamine, followed by cyclization and hydrolysis of the ester group, to give I (R = F, R1 = Cl). The latter was heated with piperazine in Me2SO to give I (R = F, R1 = 1-piperazinyl) (III). III had a min. inhibitory concentration of 50.015 mcg/mL against Escherichia coli Neum. Tablets were prepared each containing III 583.0, microcryst. cellulose 55.0, cornstarch 72.0, polyvinylpyrrolidone 30.0, dispersed silica 5.0, and Mg stearate 5.0 mg.

IT 5271-26-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (aminolysis by, of chloromethylpyridinecarboxylates)

RN 5271-26-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



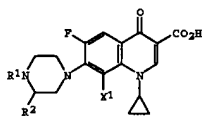
L7 ANSWER 72 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1986:186447 CAPLUS  
 DOCUMENT NUMBER: 104:186447

TITLE: 7-(3-Aryl-1-piperazinyl)- and 7-(3-cyclohexyl-1-piperazinyl)quinolone-3-carboxylic acids  
 INVENTOR(S): Petersen, Uwe; Grobe, Klaus; Zeiler, Hans Joachim; Metzger, Karl  
 PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 44 pp.  
 CODEN: GWKXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3420799	A1	19851205	DE 1984-3420799	19840604
CN 85101832	A	19870131	CN 1985-101832	19850401
CN 1014410	B	19911023		
US 4599334	A	19860708	US 1985-735493	19850517
EP 169993	A2	19860205	EP 1985-106252	19850522
EP 169993	A3	19860326		
EP 169993	B1	19881228		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 39488	E	19890115	AT 1985-106252	19850522
NO 8502063	A	19851205	NO 1985-2063	19850523
NO 165105	B	19900917		
NO 165105	C	19901227		
FI 8502205	A	19851205	FI 1985-2205	19850531
FI 82041	B	19900520		
FI 82041	C	19910110		
AU 8543206	A1	19851212	AU 1985-43206	19850531
AU 571333	B2	19880414		
JP 61001683	A2	19860107	JP 1985-116836	19850531
CA 1248954	A1	19890117	CA 1985-482912	19850531
IL 75370	A1	19890331	IL 1985-75370	19850531
IL 85549	A1	19890331	IL 1985-85549	19850531
DK 8502496	A	19851205	DK 1985-2496	19850603
DK 162527	B	19911111		
DK 162527	C	19920330		
ZA 8504168	A	19860129	ZA 1985-4168	19850603
ES 543839	A1	19860601	ES 1985-543839	19850603
HU 39175	A2	19860828	HU 1985-2145	19850603
HU 194866	B	19880328		
DD 240016	A5	19861015	DD 1985-276974	19850603
ES 552573	A1	19871011	ES 1986-552573	19860228
ES 552574	A1	19871011	ES 1986-552574	19860228
JP 66279411	A2	19941004	JP 1993-342256	19931215

PRIORITY APPL. INFO.:  
 CASREACT 104:186447

OTHER SOURCE(S):  
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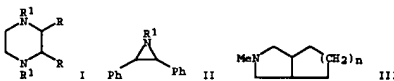
IT 5271-26-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (hydrogenation of, with ruthenium catalysts)

RN 5271-26-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 74 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1985:422404 CAPLUS  
 DOCUMENT NUMBER: 103:22404  
 TITLE: Deprotonation of aliphatic amine N-oxides: general reaction scheme and new synthesis of pyrrolidines  
 AUTHOR(S): Beugelmans, Rene; Benadjila-Iguersire, Leila; Chastanet, Jacqueline; Negron, Guillermo; Roussi, Georges  
 CORPORATE SOURCE: Inst. Chim. Subst. Nat., CNRS, Gif-sur-Yvette, 91190, Fr.  
 SOURCE: Canadian Journal of Chemistry (1985), 63(3), 725-34  
 CODEN: CJCHAG; ISSN: 0008-4042  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 OTHER SOURCE(S): CASREACT 103:22404  
 GI



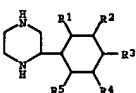
AB Amine oxides RCH2N(O)R1CH2R2 (R = Ph, R1 = Me, R2 = H, Ph; R = R2 = Ph, R1 = PhCH2; R = R2 = H, R1 = Me, Ph, 2,4,6-Me3C6H2) treated with Li (N(CMe2)2) undergo deprotonation. Monodeprotonation gives rise to RCH2CHNHR2 and R2H via hydrolysis of the intermediate immonium ion or to R2CH2CHNHR2 via a Stevens-like rearrangement. Double deprotonation gives an immonium ylide which, depending upon the structure of the initial tertiary amine yields either head to head piperazines I or aziridines II. The immonium ylide from Me2N(O) underwent cycloaddn. reactions with unactivated olefins, leading to a new and efficient synthesis of various pyrrolidines, e.g., III (n = 1,3,4).

IT 81601-99-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and methylation of)

RN 81601-99-2 CAPLUS

CN Piperazine, 2,3-diphenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

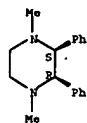


AB The title compds. [I; R1-R5 = H, alkyl, cyclohexyl, alkoxy, PhCH2O, alkoxy carbonyl, OH, halo, amino, piperidino, piperazinyl, thiasolyl, imidazolyl] were prepared by hydrogenation of phenylpiperazines over Ru catalysts supported on Al2O3 or C. Thus, 52 g 2-phenylpiperazine was hydrogenated in THF over Ru/Al2O3 at 150-160° and 160-200 bar to give 49 g I (R1-R5 = H). I are intermediates for bactericides.



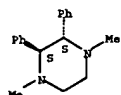
IT 81577-01-7P 81577-03-9P 96819-58-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 EN 81577-01-7 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

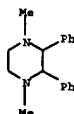


EN 81577-03-9 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



EN 96819-58-8 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-diphenyl- (9CI) (CA INDEX NAME)



IT 81502-00-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation, benzoylation, and methylation of)  
 EN 81502-00-8 CAPLUS  
 CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

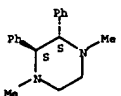
Relative stereochemistry.

IT artery in vitro.  
 5271-26-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with isoquinolinesulfonyl chloride)  
 EN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 76 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1982:582385 CAPLUS  
 DOCUMENT NUMBER: 97:182385  
 TITLE: Electrochemical reduction of di-Schiff bases.  
 Synthesis of piperazines, indolindoles, diazepines,  
 and diazocines  
 AUTHOR(S): Koch, Russell W.; Dessy, Raymond E.  
 CORPORATE SOURCE: Chem. Dep., Virginia Polytech. Inst. and State Univ.,  
 Blacksburg, VA, 24061, USA  
 SOURCE: Journal of Organic Chemistry (1982), 47(23), 4452-9  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The electrochem. reduction of a series of di-Schiff bases has led to examples  
 where products representing reduction, cyclization, and transannular  
 cyclization are found. Useful synthetic pathways for piperazines,  
 indolindoles, diazepines, and diazocines are described.  
 IT 81577-03-9P 83027-12-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 EN 81577-03-9 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



EN 83027-12-7 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, dihydrochloride, trans- (9CI) (CA INDEX NAME)

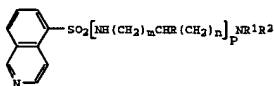
Relative stereochemistry.



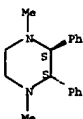
L7 ANSWER 75 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1982:71954 CAPLUS  
 DOCUMENT NUMBER: 98:71954  
 TITLE: Isoquinolinesulfonyl derivatives  
 INVENTOR(S): Hidaka, Hiroyoshi; Sone, Takanori; Sasaki, Yasuharu;  
 Sugihara, Taisuke  
 PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan  
 SOURCE: Eur. Pat. Appl., 82 pp.  
 CODEN: EPYKDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 61673	A1	19821006	EP 1982-102291	19820319
EP 61673	B1	19841024		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
JP 57156463	A2	19820927	JP 1981-39550	19810320
JP 63048869	B4	19880930		
JP 57200366	A2	19821208	JP 1981-82559	19810601
JP 63061942	B4	19881130		
JP 58121278	A2	19830719	JP 1982-2229	19820112
JP 01044188	B4	19880926		
JP 58121279	A2	19830719	JP 1982-3291	19820114
JP 02027992	B4	19900620		
US 4456757	A	19840626	US 1982-357770	19820312
US 4525589	A	19850625	US 1984-572418	19840120
US 4560755	A	19851224	US 1984-572419	19840120
PRIORITY APPL. INFO.:				
			JP 1981-39550	A 19810320
			JP 1981-82559	A 19810601
			JP 1982-2229	A 19820112
			JP 1982-3291	A 19820114
			US 1982-357770	A3 19820312

OTHER SOURCE(S): CASREACT 98:71954  
 GI



AB Isoquinolinesulfonyl derivatives I (m, n = 0-9; p = 0, 1; R = H, alkyl, cycloalkyl, aryl; R1, R2 = H, alkyl, cycloalkyl, aryl, aralkyl; NR1R2 = heterocyclic) were prepared. Thus, 5-isoquinolinesulfonyl chloride was treated with H2N(CH2)4NH2 to give 62% N-(4-aminobutyl)-5-isoquinolinesulfonyl derivative which had a vasodilator ED50 of 11 µM mesenteric



● 2 HCl

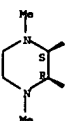
L7 ANSWER 77 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1982:492234 CAPLUS  
 DOCUMENT NUMBER: 97:92234  
 TITLE: The reactivity of benzyldimethylamine N-oxide on treatment with strong bases  
 AUTHOR(S): Beugelmans, R.; Benedjila-Iguersa, L.; Roussi, G.  
 CORPORATE SOURCE: Inst. Chim. Sub. Nat., Gif-sur-Yvette, 91190, Fr.  
 SOURCE: Journal of the Chemical Society, Chemical Communications (1982), (10), 544-5  
 CODEN: JOCCAT; ISSN: 0022-4936  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English



AB Treatment of the title compound with either BuLi in THF or LiNH2 in NH3 at -78° gave piperazines I (R = α-, β-Ph) and PhCHO.

Analogous treatment of PhCH2NMe2 gave only PhCH2NMe2. A mechanism involving biradical intermediates is proposed for the formation of I.  
 IT 81577-01-7P 81577-03-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, by reductive dimerization of benzyldimethylamine oxide)  
 EN 81577-01-7 CAPLUS  
 CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, cis- (9CI) (CA INDEX NAME)

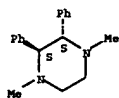
Relative stereochemistry.



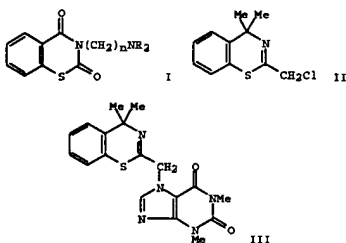
EN 81577-03-9 CAPLUS

CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L7 ANSWER 78 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1982:199608 CAPLUS  
DOCUMENT NUMBER: 96:199608  
TITLE: Synthesis and pharmacological activity of benzothiazine derivatives  
AUTHOR(S): Lopatina, E. I.; Artemenko, G. N.; Sokolova, T. V.; Avchilov, N. A.; Zagorevskii, V. A.  
CORPORATE SOURCE: Nauchno-Issled. Inst. Farm., Moscow, USSR  
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1982), 16(2), 173-6  
CODEN: KHFZAN; ISSN: 0023-1134  
DOCUMENT TYPE: Journal  
LANGUAGE: Russian  
OTHER SOURCE(S): CASREACT 96:199608  
OI

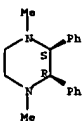


AB Alkylation of 1,3-benzothiazine-2,4-dione with NaH and Cl(CH<sub>2</sub>)<sub>n</sub>NR<sub>2</sub> gave 60-44% I (n, R = 2, Me, 3, Me, 2, Et). Cycloaddn. of 2-PhCH<sub>2</sub>SC<sub>6</sub>H<sub>4</sub>CM<sub>2</sub>OH with ClCH<sub>2</sub>CN gave II, which was aminated with heterocyclic amines or alkylated with AcNHCH(CO<sub>2</sub>Et)<sub>2</sub>. Of the compds. prepared, xanthinyl derivative III had the greatest antidepressant activity.  
IT 5368-28-5  
RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with (chloromethyl)dimethylbenzothiazine)  
EN 5368-28-5 CAPLUS  
CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



IT 81577-01-7 81601-99-2  
RL: RCT (Reactant); RACT (Reactant or reagent) (photochem. isomerization of)  
EN 81577-01-7 CAPLUS  
CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



EN 81601-99-2 CAPLUS  
CN Piperazine, 2,3-diphenyl-, cis- (9CI) (CA INDEX NAME)

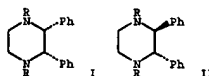
Relative stereochemistry.



L7 ANSWER 80 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1979:456177 CAPLUS  
DOCUMENT NUMBER: 91:56177  
TITLE: Aminophosphine-rhodium complexes as catalysts in asymmetric hydrogenation. The dependence of the enantioselectivity on the structure of the chiral ligands  
AUTHOR(S): Fiorini, M.; Giomgo, G. M.  
CORPORATE SOURCE: ASSOREMI-Lab. Processi Microbiol., Monterotondo, 06015, Italy  
SOURCE: Journal of Molecular Catalysis (1979), 5(4), 303-10  
CODEN: JMCADS; ISSN: 0304-5102  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB An investigation of the title asym. catalysts was extended to a series of structurally different chiral bis-aminophosphine ligands. The results, albeit restricted to a limited number of representative substrates, show that the catalyst enantioselectivity is markedly influenced, and in some cases substantially improved, by the chemical modification of the chelate ligand structure.  
IT 70708-34-8P

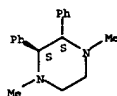


L7 ANSWER 79 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1982:180416 CAPLUS  
DOCUMENT NUMBER: 96:180416  
TITLE: Photochemical cis, trans-isomerization in the 2,3-diphenylpiperazine series  
AUTHOR(S): Benadilla-Ignaterra, L.; Chastanet, J.; Roussi, G.  
CORPORATE SOURCE: Inst. Chim. Subst. Nat., CNRS, Gif-sur-Yvette, 91190, Fr.  
SOURCE: Heterocycles (1982), 19(2), 213-15  
CODEN: HETCYM; ISSN: 0385-5414  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 96:180416  
OI



AB Photolysis of I (R = H, Me) in MeCN gave II; I (R = CH<sub>2</sub>Ph) failed to isomerize. Under the same conditions II did not isomerize. Sensitization and quenching expts. with I (R = Me) suggested that isomerization proceeded via the singlet excited state.  
IT 81577-03-9 81602-00-8  
RL: RCT (Reactant); RACT (Reactant or reagent) (attempted photochem. isomerization of)  
EN 81577-03-9 CAPLUS  
CN Piperazine, 1,4-dimethyl-2,3-diphenyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



EN 81602-00-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction with halo diphenylphosphine)  
EN 70708-34-8 CAPLUS  
CN Piperazine, 2,3-diphenyl-, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 81 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1979:168547 CAPLUS  
DOCUMENT NUMBER: 90:168547  
TITLE: Synthesis of N-(2-piperazinoethyl)propionanilides  
AUTHOR(S): Okada, Jutaru; Shimabayashi, Masaharu  
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, Japan  
SOURCE: Yakugaku Zasshi (1978), 98(12), 1619-28  
CODEN: YKKEAJ; ISSN: 0031-6903  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese  
OTHER SOURCE(S): CASREACT 90:168547  
OI



AB Aminating PhNHCHE<sup>1</sup>CH<sub>2</sub>Br.HBr (R = H; R<sup>1</sup> = H, Me) with I (R<sup>2</sup> = H, Me, Ph; R<sup>3</sup> = Me, Et, PhCH<sub>2</sub>, PhCH<sub>2</sub>CH<sub>2</sub>) gave II (R = H), which were N-acylated with (EtCO)<sub>2</sub>O to give II (R = EtCO). Treating PhNHCHE<sup>1</sup>CH<sub>2</sub>Br with I (R<sup>2</sup> = H, R<sup>3</sup> = Me) (III) followed by LiAlH<sub>4</sub> reduction gave II (R<sup>2</sup> = H; R<sup>3</sup> = Me) in an overall yield (35.3%) lower than that (55.6%) by one-step amination of PhNHCHE<sup>1</sup>CH<sub>2</sub>Br.HBr with III. The analgesic activity of II (R = EtCO; R<sup>1</sup> = R<sup>3</sup> = Me, R<sup>2</sup> = H) was about 1/9 of that of morphine. The Me or Ph group at the 3 position of piperazine ring decreased the analgesic activity.  
IT 5368-33-2  
RL: RCT (Reactant); RACT (Reactant or reagent) (N-alkylation of, by bromoethylamine)  
EN 5368-33-2 CAPLUS  
CN Piperazine, 2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



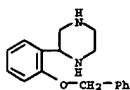
L7 ANSWER 82 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1978:89714 CAPLUS  
 DOCUMENT NUMBER: 89:89714  
 TITLE: 2-arylpiperazine derivatives  
 INVENTOR(S): Kato, Hideo; Koshinaka, Eiichi; Ogawa, Nobuo  
 PATENT ASSIGNEE(S): Hakuriku Pharmaceutical Co., Ltd., Japan  
 SOURCE: Ger. Offen., 10 pp.  
 CODEN: GWKMBY  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2718451	A1	19771201	DE 1977-2718451	19770426
JP 52139085	A2	19771119	JP 1976-53865	19760513
JP 56027508	B4	19810625		
US 4166180	A	19790828	US 1977-795869	19770511
GB 1519747	A	19780802	GB 1977-20028	19770512
FR 2351108	A1	19771209	FR 1977-14800	19770513
FR 2351108	B1	19800118		
			JP 1976-53865	A 19760513

PRIORITY APPLN. INFO.:  
 GI



AB Arylpiperazines I (R = Ph, optionally substituted by 1-3 halogen, lower alkyl or alkoxy, NO<sub>2</sub>, CN, OCH<sub>2</sub>Ph, or OH, methylenedioxyphenyl) were prepared. Thus 3-PhCH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>Ac was oxidized with SeO<sub>2</sub>, 3-PhCH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>COCH<sub>3</sub> treated with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> to give I (R = 3-PhCH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>), which was hydrogenated over Pd-C to give I (R = 3-HOC<sub>6</sub>H<sub>4</sub>). I had analgesic, vasodilator, and spasmolytic activity, as well as an effect on the circulation (no data).  
 IT 65709-49-19  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and debenzoylation of)  
 RN 65709-49-1 CAPLUS  
 CN Piperazine, 2-(2-(phenylmethoxy)phenyl)- (9CI) (CA INDEX NAME)

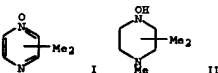


IT 65709-26-49 65709-27-55 65709-28-6P  
 65709-50-49 65709-59-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 65709-26-4 CAPLUS



●2 HCl

L7 ANSWER 83 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1978:74373 CAPLUS  
 DOCUMENT NUMBER: 88:74373  
 TITLE: Quaternization of pyrazine monoxides, and reduction of 1-methyl-4-oxidopyrazinium iodides with sodium borohydride  
 AUTHOR(S): Ohno, Akihiko; Matsunaga, Mayumi; Iwata, Noriko; Watanabe, Tokuhiko  
 CORPORATE SOURCE: Tokyo Coll. Pharm., Tokyo, Japan  
 SOURCE: Heterocycles (1977), 8, 351-6  
 CODEN: HTCYAM; ISSN: 0385-5414  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 88:74373  
 GI



AB Dimethylpyrazine monoxides I (4 isomers) and 2,3-diphenylpyrazine 1-oxide were quaternized by treatment with MeI in a sealed tube for 2 h at 80°. 3-Phenyl-, 2,5-diphenyl-, and 3,5-diphenylpyrazine 1-oxides could not be quaternized. Reduction of the oxidopyrazinium iodides with NaBH<sub>4</sub> gave the corresponding 1-hydroxypiperazines, e.g., II.  
 IT 65464-26-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 65464-26-8 CAPLUS  
 CN Piperazine, 1-methyl-2,3-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 84 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1977:453214 CAPLUS  
 DOCUMENT NUMBER: 87:53214

CN Piperazine, 2-(2-chlorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 65709-27-5 CAPLUS  
 CN Piperazine, 2-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

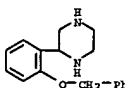


RN 65709-28-6 CAPLUS  
 CN Piperazine, 2-(2-methoxyphenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

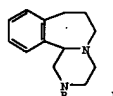
RN 65709-50-4 CAPLUS  
 CN Piperazine, 2-[(2-(phenylmethoxy)phenyl)-], dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 65709-59-3 CAPLUS  
 CN Phenol, 2-(2-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)

TITLE: Agents acting on the central nervous system: Part XIV. 2-Substituted 1,2,3,4,6,7,8,12b-octahydropyrazino[2,1-a][2]benzazepines  
 AUTHOR(S): Dixit, V. M.; Khanna, J. M.; Anand, Nitya  
 CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, India  
 SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1976), 14B(11), 874-8  
 CODEN: IJSEDB; ISSN: 0376-4699  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 87:53214  
 GI



AB 3-Oxo-2-phenylpiperazine was treated with BrCH<sub>2</sub>CH<sub>2</sub>COCl and the 1-(3-bromopropionyl)-3-oxo-2-phenylpiperazine cyclized with AlCl<sub>3</sub> followed by LiAlH<sub>4</sub> reduction to give the pyrazinobenzazepine I (R = H), which was alkylated to give I (R = PhCH<sub>2</sub>CH<sub>2</sub>, PhCH(OH)CH<sub>2</sub>, 4-pyridylethyl, p-FC<sub>6</sub>H<sub>4</sub>CO(CH<sub>2</sub>)<sub>3</sub>, CH<sub>2</sub>CN, MeCO(CH<sub>2</sub>)<sub>2</sub>, 4,5-dihydro-2-imidazolylmethyl). I (R = H) had trans stereochem.  
 IT 5271-26-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction with ethyl bromide)  
 RN 5271-26-1 CAPLUS  
 CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT 5368-28-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with bromopropionyl chloride)  
 RN 5368-28-5 CAPLUS  
 CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)

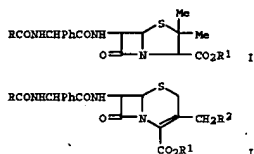


L7 ANSWER 85 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1976:432052 CAPLUS

DOCUMENT NUMBER: 85:33052  
 TITLE: Penicillin and cephalosporin derivatives  
 INVENTOR(S): Saikawa, Isamu; Takano, Shuntaro; Yoshida, Chomaku; Takashima, Okuta; Mochimaru, Kaishu; Kuroda, Seisaku; Komatsu, Miwako; Yasuda, Takashi; Kodama, Yutaka  
 PATENT ASSIGNER(S): Toyama Chemical Co., Ltd., Japan  
 SOURCE: Ger. Offen., 237 pp.  
 CODEN: GWKXBY  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2519400	A1	19760304	DE 1975-2519400	19750430
DE 2519400	B2	19810521		
DE 2519400	C3	19820211		
JP 50149378	A2	19751127	JP 1974-50663	19740509
JP 50149380	A2	19751127	JP 1974-52254	19740513
JP 50151891	A2	19751206	JP 1974-60787	19740531
JP 51023204	A2	19760324	JP 1974-91996	19740813
JP 51039687	A2	19760402	JP 1974-109954	19740926
JP 51070788	A2	19760610	JP 1974-142499	19741213
JP 51113890	A2	19761007	JP 1975-37207	19750327
AT 7608289	A	19771215	AT 1976-8289	19761108
ES 454266	A1	19771216	ES 1976-454266	19761215
ES 454267	A1	19771216	ES 1976-454267	19761215
US 4379152	A	19804005	US 1979-39904	19790517
PRIORITY APPL. INFO.:				
			JP 1974-50663	A 19740509
			JP 1974-52254	A 19740513
			JP 1974-60787	A 19740531
			JP 1974-91996	A 19740813
			JP 1974-109954	A 19740926
			JP 1974-142499	A 19741213
			JP 1975-37207	A 19750327
			AT 1975-3511	A 19750507
			US 1976-654060	A3 19760130
			US 1978-915873	A3 19780615

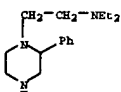
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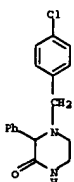
AB Acylaminobenzylpenams I and -cephems II (R = substituted oxopiperazino; R1 = H, Na, ester; R2 = H, OAc, heterocyclic thiol) (164 compds.) were prepared by acylating aminobenzylpenams and -cephems. Thus 1-acetyl-3-oxopiperazine was treated with COCl2 and used to acylate ampicillin to I (R = 4-acetyl-2-oxopiperazino, R1 = Na).  
 IT 5368-28-5



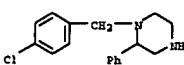
IT 26921-23-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and alkylation of)  
 RN 26921-23-3 CAPLUS  
 CN 1-Piperazineethanamine, N,N-diethyl-2-phenyl- (9CI) (CA INDEX NAME)



IT 26840-79-9P 26840-82-4F 26840-87-9P  
 26840-93-7F 26840-97-1F 59622-60-5P  
 59622-61-6F 59622-62-7F 59622-77-4P  
 59622-82-1F 59622-88-7F 59622-90-1P  
 59622-94-5P 59622-98-9F 59623-00-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and aminoalkylation of)  
 RN 26840-79-9 CAPLUS  
 CN Piperazinone, 4-[(4-chlorophenyl)methyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 26840-82-4 CAPLUS  
 CN Piperazine, 1-[(4-chlorophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



RN 26840-87-9 CAPLUS

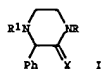
RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with phosgene)  
 RN 5368-28-5 CAPLUS  
 CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 86 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
 ACCESSION NUMBER: 1976:421459 CAPLUS  
 DOCUMENT NUMBER: 65:21459  
 TITLE: The 2- or 3-keto-3- or -2-phenyl-1,4-disubstituted piperazines  
 INVENTOR(S): Zellner, Hugo  
 PATENT ASSIGNER(S): Donau-Pharmazie G.m.b.H., Austria  
 SOURCE: U.S., 29 pp.  
 CODEN: USKXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3935214	A	19760127	US 1973-333497	19730220
AT 284127	B	19700910	AT 1968-7306	19680726
US 4012389	A	19770315	US 1975-627690	19751031
PRIORITY APPL. INFO.:				
			AT 1968-7306	A 19680726
			US 1969-048395	A2 19690723
			US 1973-333497	A3 19730220

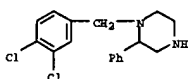
GI



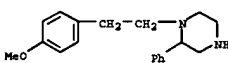
AB The piperazines I (R = Et2NCH2CH2, 2-piperidinoethyl, bis(morpholinomethyl)methyl, 4-MeOC6H4CH2, ClCH2CH2, 2-morpholinoethyl, etc.; R1 4-ClC6H4CH2, 2,4-Cl2C6H3CH2, 4-MeOC6H4CH2CH2, Ph(CH2)3, Et2NCH2CH2, 4-EtOC6H4CH2, etc.; X = O, R2) were prepared by alkylation of piperazine derivs. Thus, 2-phenyl-3-oxopiperazine was treated with 4-ClC6H4CH2Cl to give I (R = H, R1 = 4-ClC6H4CH2, X = O), which was treated with Et2NCH2CH2Cl to give I (R = Et2NCH2CH2, R1 = 4-ClC6H4CH2, X = O) (II). At 1 mM I had a blood coagulation promoting effect and at 5 mM had a blood coagulation inhibiting effect.  
 IT 5368-28-5

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (alkylation of)  
 RN 5368-28-5 CAPLUS  
 CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)

CN Piperazine, 1-[(3,4-dichlorophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



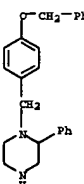
RN 26840-93-7 CAPLUS  
 CN Piperazine, 1-(2-(4-methoxyphenyl)ethyl)-2-phenyl- (9CI) (CA INDEX NAME)



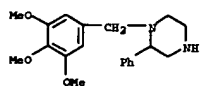
RN 26840-97-1 CAPLUS  
 CN Piperazine, 2-phenyl-1-(3-phenylpropyl)- (8CI, 9CI) (CA INDEX NAME)



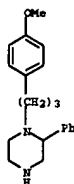
RN 59622-60-5 CAPLUS  
 CN Piperazine, 2-phenyl-1-[(4-(phenylmethoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



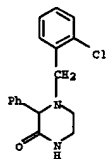
RN 59622-61-6 CAPLUS  
 CN Piperazine, 2-phenyl-1-[(3,4,5-trimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



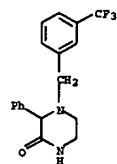
RN 59622-62-7 CAPLUS  
CN Piperazine, 1-[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



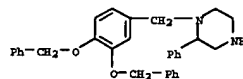
RN 59622-77-4 CAPLUS  
CN Piperazine, 1-[[3,4-bis(phenylmethoxy)phenyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)



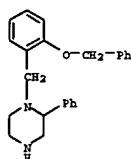
RN 59622-82-1 CAPLUS  
CN Piperazine, 1-[[3-(trifluoromethyl)phenyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)



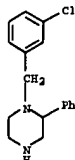
RN 59622-88-7 CAPLUS  
CN Piperazine, 1-[[3,4-bis(phenylmethoxy)phenyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)



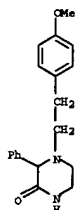
RN 59622-90-1 CAPLUS  
CN Piperazine, 2-phenyl-1-[[2-(phenylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



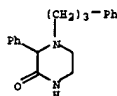
RN 59622-94-5 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



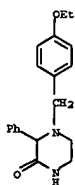
NAME)



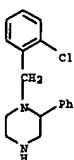
RN 26840-96-0 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



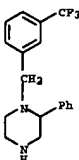
RN 59622-55-8 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



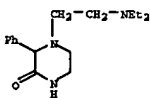
RN 59622-56-9 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



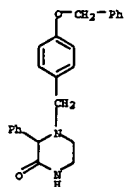
RN 59622-00-6 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



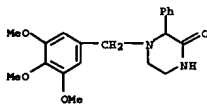
IT 26840-81-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reactions of)  
RN 26840-81-3 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



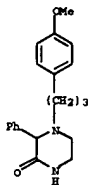
IT 26840-92-6P 26840-96-0F 59622-55-8P  
59622-56-9P 59622-57-0F 59622-58-1P  
59622-87-6P 59622-89-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reduction of)  
RN 26840-92-6 CAPLUS  
CN Piperazine, 1-[[3-(4-methoxyphenyl)propyl]-2-phenyl- (9CI) (CA INDEX NAME)



RN 59622-57-0 CAPLUS  
CN Piperazine, 3-phenyl-4-[(3,4,5-trimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

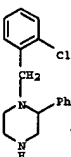


RN 59622-58-1 CAPLUS  
CN Piperazine, 4-[(3-(4-methoxyphenyl)propyl)-3-phenyl]- (9CI) (CA INDEX NAME)



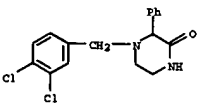
RN 59622-57-6 CAPLUS  
CN Piperazine, 4-[(3,4-bis(phenylmethoxy)phenyl)methyl]-3-phenyl- (9CI) (CA INDEX NAME)

INDEX NAME)

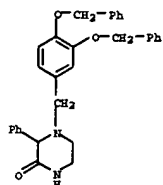
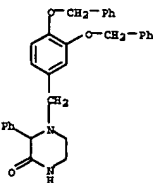


●x HCl

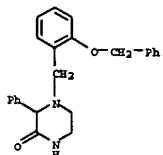
IT 26840-86-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation reduction of)  
RN 26840-86-8 CAPLUS  
CN Piperazine, 4-[(3,4-dichlorophenyl)methyl]-3-phenyl- (9CI) (CA INDEX NAME)



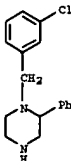
IT 59622-87-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reduction of)  
RN 59622-87-6 CAPLUS  
CN Piperazine, 4-[(3,4-bis(phenylmethoxy)phenyl)methyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 59622-89-8 CAPLUS  
CN Piperazine, 3-phenyl-4-[(2-(phenylmethoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



IT 59622-95-6F 59622-97-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 59622-95-6 CAPLUS  
CN Piperazine, 1-[(2-chlorophenyl)methyl]-2-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 59622-97-8 CAPLUS  
CN Piperazine, 1-[(2-chlorophenyl)methyl]-2-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

L7 ANSWER 97 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1976:4904 CAPLUS  
DOCUMENT NUMBER: 84:4904  
TITLE: N-Alkylation of secondary amines with esters and lithium alanate (lithium aluminum hydride)  
AUTHOR(S): Khanna, J. M.; Dixit, V. M.; Anand, Nitya  
CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, India  
SOURCE: Synthesis (1975), (9), 607-8  
CODEN: SYNTRF; ISSN: 0039-7881  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 84:4904  
AB 1-Phenyl-, 2-phenyl-, 1-methylpiperazine, piperidine, and PhCH2NHMe were N-alkylated by reaction with RCO2Et (R = H, Me, Et) and LiAlH4 in THF or ether. Thus, reaction of 1-phenylpiperazine with RCO2Et and LiAlH4 gave 4-methyl-1-phenylpiperazine in 90% yield. 2-Phenylpiperazine with AcOEt and LiAlH4 gave 80% 4-ethyl-2-phenylpiperazine. A mechanism, involving initial carboxamide formation and its LiAlH4 reduction to the tertiary amine, was suggested.  
IT 5271-26-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(B-ethylation of, with ethyl acetate and lithium aluminum hydride)  
RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT 5368-28-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Reaction of, with methyl or ethyl acetate and lithium aluminum hydride)  
RN 5368-28-5 CAPLUS  
CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 98 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1975:428282 CAPLUS  
DOCUMENT NUMBER: 83:28282  
TITLE: 1-Adamantylcarbonyl-3,3-diphenylpiperazines  
INVENTOR(S): Freed, Meier E.; Childress, Scott J.  
PATENT ASSIGNEE(S): American Home Products Corp., USA  
SOURCE: U.S., 9 pp. Division of U.S. 3,749,725 (CA 79:105298k).  
CODEN: USXKAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
.....	.....	.....	.....	.....

US 3869460 A 19750304 US 1973-347940 19730404  
US 3749725 A 19730731 US 1971-161322 19710709  
PRIORITY APPLN. INFO.: US 1971-161322 A3 19710709  
US 1968-786367 A3 19681223

GI For diagram(s), see printed CA Issue.  
AB Piperazines (I, R = 1-adamantylcarbonyl, alkyl, aminoalkyl, alkanoyl, phenylalkyl etc. X = O, H2) were prepared. Thus, 2,2-diphenylpiperazine was refluxed with 1-adamantanecarbonyl chloride in Me2CO-Et3N to give I (R = 1-adamantanecarbonyl, X = H2). I were mydriatic agents when tested in mice at 4-400 mg/kg.  
IT 35676-88-1P 41353-93-9F 49662-87-5P  
49662-90-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 35676-88-1 CAPLUS  
CN Piperazine, 1-methyl-3,3-diphenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 41353-93-9 CAPLUS  
CN Piperazine, 2,2-diphenyl- (9CI) (CA INDEX NAME)

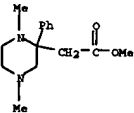


RN 49662-87-5 CAPLUS  
CN Piperazine, 2,2-diphenyl-, dihydrochloride (9CI) (CA INDEX NAME)

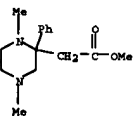


● 2 HCl

RN 49662-90-0 CAPLUS  
CN Piperazine, 1-methyl-3,3-diphenyl- (9CI) (CA INDEX NAME)

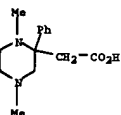


RN 51212-12-5 CAPLUS  
CN 2-Piperazineacetic acid, 1,4-dimethyl-2-phenyl-, methyl ester, dihydrochloride (9CI) (CA INDEX NAME)



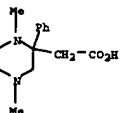
● 2 HCl

RN 51212-17-0 CAPLUS  
CN 2-Piperazineacetic acid, 1,4-dimethyl-2-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 51271-01-3 CAPLUS  
CN 2-Piperazineacetic acid, 1,4-dimethyl-2-phenyl- (9CI) (CA INDEX NAME)



IT 22476-76-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reduction and reaction of, with dimethylaminopropyl chloride)  
RN 22476-76-2 CAPLUS  
CN Piperazinone, 3,3-diphenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 89 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1974:425642 CAPLUS  
DOCUMENT NUMBER: 81:25642  
TITLE: Synthesis of aryl-substituted 1,3- and 1,4-diazocine derivatives  
AUTHOR(S): Sarges, Reinhard; Tretter, James R.  
CORPORATE SOURCE: Cent. Res., Pfizer Inc., Groton, CT, USA.  
SOURCE: Journal of Organic Chemistry (1974), 39(12), 1710-16  
CODEN: JOCEAH; ISSN: 0022-3263  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 81:25642  
GI For diagram(s), see printed CA Issue.  
AB The synthesis of aryl-substituted 1,3- and 1,4-diazocine deriva. was undertaken because their structural features suggested potential central nervous system activity. Reaction of Me  $\beta$ -(bromomethyl)cinnamate with N,N'-dimethylethylene-diamine gave Me N,N'-dimethyl-2-phenylpiperazine-2-acetate which was converted to 1,4-dimethyl-7-phenyl-1,2,3,4-tetrahydro-1,4-diazocin-5(8H)-one (I). Catalytic and hydride reduction of I led ultimately to the 6-phenylperhydro-1,4-diazocine (II). Conversion of trans-3-phenylproline to III followed by desulfurization and quaternization with MeI gave the bicyclic intermediate IV, which on treatment with NaOH or Li-NH3 underwent transannular ring opening to give 1,3-dimethyl-6-phenyl-1,2,3,7-tetrahydro-1,3-diazocin-4(8H)-one (IV) and its perhydro analog. resp. Reaction of IV with NaOMe or with NaBH4 led to peripheral ring cleavage giving N-methyl-3-phenylproline methyl ester and the corresponding alc., resp.  
IT 51212-11-4F 51212-12-5F 51212-17-0P  
51271-01-3F  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 51212-11-4 CAPLUS  
CN 2-Piperazineacetic acid, 1,4-dimethyl-2-phenyl-, methyl ester (9CI) (CA INDEX NAME)

L7 ANSWER 90 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1974:425574 CAPLUS  
DOCUMENT NUMBER: 81:25574  
TITLE: 3-(1,2,3,4-Tetrahydroisoquinolinomethyl)-3-quinuclidinol and related compounds  
INVENTOR(S): Potoski, John R.; Freed, Meier E.  
PATENT ASSIGNER(S): American Home Products Corp.  
SOURCE: U.S. 8 pp. Division of U.S. 3,725,410 (CA 79:5367r).  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3792053	A	19740212	US 1972-278663	19720807
US 3725410	A	19730403	US 1970-55264	19700715
			US 1970-55264	A 19700715

PRIORITY APPLN. INFO.:  
GI For diagram(s), see printed CA Issue.  
AB Ten quinuclidinole I (R = 4-phenyl-1-piperaziny, 3,3-diphenyl-1-piperaziny, 4-phenylpiperidino, Et2N, morpholino, 1,2,3,4-tetrahydro-2-isoquinolinyl, etc.) were prepared by treating 3-methylenequinuclidine oxide (II) with amines. II was prepared from 3-quinuclidinone and trimethylsulfoxonium iodide. At 4-400 mg/kg I decreased the motor activity of mice. At 10 ml/kg I reduced carrageenin induced by edema by 23%.  
IT 41353-93-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with 3-methylenequinuclidine oxide)  
RN 41353-93-9 CAPLUS  
CN Piperazine, 2,2-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 91 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1974:70721 CAPLUS  
DOCUMENT NUMBER: 80:70721  
TITLE: 3-[(1S)-Asapiro[5.5]undecino]methyl-3-quinuclidinol  
INVENTOR(S): Potoski, John R.; Freed, Meier E.  
PATENT ASSIGNER(S): American Home Products Corp.  
SOURCE: U.S., 8 pp. Division of U.S. 3,725,410 (CA 79:5367r).  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3775418	A	19731127	US 1972-278664	19720807
US 3725410	A	19730403	US 1970-55264	19700715

PRIORITY APPLN. INFO.:  
GI For diagram(s), see printed CA Issue. A3 19700715

AB Central depressant and antiinflammatory quinolidinol deriva. I (NRR1 = 4-phenyl-1-piperazinyl, 3,3-diphenyl-1-piperazinyl, 4-phenylpiperidino, 4,4-spiropentamethylenepiperidino, 1,2,3,4-tetrahydro-1-isoquinolinyl, NRR2, NRR3, CH2CH2NRR2, morpholino) were prepared by treating 3-quinolidinone with Me2S(O)Me-I- and NaH and treating the resulting spirooxiranequinolidine with the amine.

IT 41353-93-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with spirooxiranequinolidine)

EN 41353-93-9 CAPLUS

CN Piperazine, 2,2-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 92 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1974:70719 CAPLUS  
DOCUMENT NUMBER: 80:70719  
TITLE: 3-Methylenequinolidine oxide  
INVENTOR(S): Potoski, John R.; Freed, Meier E.  
PATENT ASSIGNEE(S): American Home Products Corp.  
SOURCE: U.S., 8 pp. Division of U.S. 3,725,410 (CA 79:5367r).  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3775419	A	19731127	US 1972-278690	19720807
US 3775410	A	19730403	US 1970-55264	19700715

PRIORITY APPLN. INFO.:  
GI For diagram(s), see printed CA Issue.

AB The spirooxiranequinolidine I was prepared by treating 3-quinolidinone with Me2S(O)Me-I- and NaH. It is an intermediate for the central depressant and antiinflammatory quinolidinols II (NRR1 = 4-phenyl-1-piperazinyl, 3,3-diphenyl-1-piperazinyl, 4-phenylpiperidino, 4,4-spiropentamethylenepiperidino, 1,2,3,4-tetrahydro-1-isoquinolinyl, NRR2, NRR3, CH2CH2NRR2, morpholino), which were prepared by treating I with R2NH.

IT 41353-93-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with spirooxiranequinolidine)

EN 41353-93-9 CAPLUS

CN Piperazine, 2,2-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 93 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN



EN 49662-87-5 CAPLUS  
CN Piperazine, 2,2-diphenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

EN 49662-90-0 CAPLUS  
CN Piperazine, 1-methyl-3,3-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 94 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1973:405367 CAPLUS  
DOCUMENT NUMBER: 79:5367  
TITLE: 3-(Aminomethyl)-3-quinolidinol  
INVENTOR(S): Potoski, John R.; Freed, Meier E.  
PATENT ASSIGNEE(S): American Home Products Corp.  
SOURCE: U.S., 11 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3725410	A	19730403	US 1970-55264	19700715
US 3775418	A	19731127	US 1972-278664	19720807
US 3775419	A	19731127	US 1972-278690	19720807
US 3792053	A	19740212	US 1972-278663	19720807

PRIORITY APPLN. INFO.:  
GI For diagram(s), see printed CA Issue.

AB Quinolidinol (I) with central nervous system-depressant and antiinflammatory properties are prepared by reaction of 3-methylenequinolidine oxide (II) with heterocyclic and alkyl amines. Thus, a mixture of II and N-phenylpiperazine is heated overnight to yield I

ACCESSION NUMBER: 1973:505296 CAPLUS  
DOCUMENT NUMBER: 79:105296  
TITLE: Substituted 2,2-diphenylpiperazines and 3,3-diphenyl-2-piperazines  
INVENTOR(S): Freed, Meier E.; Childress, Scott J.  
PATENT ASSIGNEE(S): American Home Products Corp.  
SOURCE: U.S., 7 pp. Division of U.S. 3,631,047 (CA 76:99713p).  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3749725	A	19730731	US 1971-161322	19710709
US 3631047	A	19711228	US 1968-786367	19681223
US 3869460	A	19750304	US 1973-347940	19730404

PRIORITY APPLN. INFO.:  
US 1968-786367 A3 19681223  
US 1971-161322 A3 19710709

GI For diagram(s), see printed CA Issue.  
AB 2,2-Diphenylpiperazines I, R = o.g., H, CO2Et, Me, CH2CH2Ph, (CH2)3NMe2, X = H2, O useful as sympathomimetic agents were prepared by alkylating or acylating 2,2-diphenylpiperazine or 3,3-diphenyl-2-piperazine, optionally followed by reduction. Thus, I (R = H, X = H2) was treated with ClCO2Et in Et3N to give I (R = CO2Et, X = H2). This on reduction with LiAlH4 in THF gave I (R = Me, X = H2).

IT 22476-76-2F 35676-88-1F 41353-93-9P  
49662-87-5P 49662-90-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

EN 22476-76-2 CAPLUS  
CN Piperazine, 3,3-diphenyl- (8CI, 9CI) (CA INDEX NAME)



EN 35676-88-1 CAPLUS  
CN Piperazine, 1-methyl-3,3-diphenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

EN 41353-93-9 CAPLUS  
CN Piperazine, 2,2-diphenyl- (9CI) (CA INDEX NAME)

(R = 4-phenylpiperazino). Also prepared are I (R = 3,3-diphenylpiperazino, 4-phenylpiperidino, Et2N, morpholino) and 3 addnl. compds.

IT 41353-93-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with methylenequinolidine oxide)

EN 41353-93-9 CAPLUS

CN Piperazine, 2,2-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 95 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1972:99713 CAPLUS  
DOCUMENT NUMBER: 76:99713  
TITLE: Substituted 3,3-diphenylpiperazines and 3,3-diphenylpiperazin-2-ones  
INVENTOR(S): Freed, Meier E.; Childress, Scott J.  
PATENT ASSIGNEE(S): American Home Products Corp.  
SOURCE: U.S., 7 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3631047	A	19711228	US 1968-786367	19681223
US 3749725	A	19730731	US 1971-161322	19710709

PRIORITY APPLN. INFO.:  
US 1968-786367 A3 19681223

GI For diagram(s), see printed CA Issue.

AB The title compds. (I), effective sympathomimetic agents at 4-127 mg/kg in mice, were prepared by alkylation, acylation, and reduction. Thus, a mixture of I

(R = H, R1 = 2H, Ar = Ph) (II), Ph(CH2)2Br, and Et3N in PhMe was refluxed 24 hr to give I (R = Ph(CH2)2, R1 = 2H, Ar = Ph). The 2-oxo derivative (I, R = H, R1 = O, Ar = Ph) (III) was alkylated with alkyl chloride in NaH-DMP. II was acylated with ClCO2Et and Et3N in Et2O to give I (R = EtCO2, R1 = 2H, Ar = Ph), which was reduced with LiAlH4 to I (R = Me, R1 = 2H, Ar = Ph). III was also reduced with LiAlH4 to give II. Approx. 106 compds. were prepared.

IT 35676-86-9F 35676-88-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

EN 35676-86-9 CAPLUS  
CN Piperazine, 1-methyl-3,3-diphenyl-, dihydrochloride (9CI) (CA INDEX NAME)



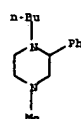
● 2 HCl

RN 35676-88-1 CAPLUS  
CN Piperazine, 1-methyl-3,3-diphenyl-, monohydrochloride (9CI) (CA INDEX NAME)

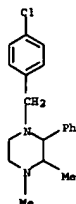


● HCl

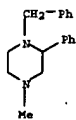
L7 ANSWER 96 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1971:74701 CAPLUS  
DOCUMENT NUMBER: 74:74701  
TITLE: Piperazine compounds. VI. Antihistaminic and anticholinergic effects of 2-phenylpiperazine derivatives  
AUTHOR(S): Ikeda, Yoshiaki; Nitta, Yoshihiro; Hirano, Isayo; Noda, Kuniko; Yamada, Kiyoshi  
CORPORATE SOURCE: Re. Lab., Chugai Pharm. Co., Ltd., Tokyo, Japan  
SOURCE: Yakugaku Zasshi (1970), 90(11), 1452-6  
CODEN: YKKZAJ; ISSN: 0031-6903  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese  
GI For diagram(s), see printed CA Issue.  
AB 1-(p-Chlorobenzyl)-2-phenyl-4-methylpiperazine (I) exhibited the most potent antihistaminic activity among 11 2-phenylpiperazines when tested in guinea pig ileum; the activity of I was less potent by a factor of approx. 10 than that of diphenylamine and cyclizine. Anticholinergic activity of I was not significant.  
IT 22287-90-7 22287-93-0 23174-98-3  
23174-99-4 23175-00-0 23175-14-6  
BL: PROC (Process)  
(antihistaminic action of)  
RN 22287-90-7 CAPLUS  
CN Piperazine, 1-butyl-4-methyl-2-phenyl- (8CI, 9CI) (CA INDEX NAME)



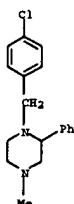
RN 22287-93-0 CAPLUS  
CN Piperazine, 1-[(4-chlorophenyl)methyl]-3,4-dimethyl-2-phenyl- (9CI) (CA INDEX NAME)



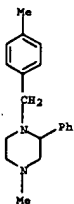
RN 23174-98-3 CAPLUS  
CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



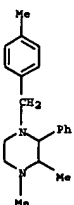
RN 23174-99-4 CAPLUS  
CN Piperazine, 1-[(4-chlorophenyl)methyl]-4-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 23175-00-0 CAPLUS  
CN Piperazine, 4-methyl-1-(p-methylbenzyl)-2-phenyl- (8CI) (CA INDEX NAME)



RN 23175-14-6 CAPLUS  
CN Piperazine, 1,2-dimethyl-4-(p-methylbenzyl)-3-phenyl- (8CI) (CA INDEX NAME)



L7 ANSWER 97 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1970:100750 CAPLUS

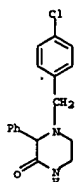
DOCUMENT NUMBER: 72:100750  
TITLE: 1,4-Substituted phenylpiperazines  
INVENTOR(S): Zellner, Hugo; Zellner, Gertraud  
PATENT ASSIGNER(S): Donau-Pharmazie G.m.b.H.  
SOURCE: Ger. Offen., 28 pp.  
CODEN: GWYKBY  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1937811	A	19700128	DE 1969-1937811	19690725
AT 284127	B	19700910	AT 1968-7306	19680726
CH 520693	A	19720331	CH 1969-520693	19690719
CH 537936	A	19730731	CH 1971-15824	19690718
CH 540268	A	19730928	CH 1971-15823	19690718
BE 736520	A	19691231	BE 1969-736520	19690724
GB 1266780	A	19720315	GB 1969-1266780	19690724
BL 6911484	A	19700128	BL 1969-11484	19690725
FR 2013813	A5	19700410	FR 1969-25493	19690725
DK 121955	B	19711227	DK 1969-4054	19690725
SE 355264	B	19730416	SE 1969-10551	19690725
CA 963904	A1	19750304	CA 1969-57953	19690725
PRIORITY APPLN. INFO.:			AT 1968-7306	A 19680726

GI For diagram(s), see printed CA Issue.  
AB The title compds. (I) blood anticoagulants, are prepared Thus, 175 g of 2-phenyl-3-oxopiperazine is treated with 177 g p-chlorobenzyl chloride and 420 ml Et3N in 2 l. Me2CO under reflux to give 65% 1-(4-chlorobenzyl)-2-phenyl-3-oxopiperazine (II) m. 175°. A mixture of 60 g II, 40 g Et2NCH2CH2Cl, and 40 g K2CO3 in 400 ml PhMe is refluxed 10 hr to give 90% 1-(4-chlorobenzyl)-2-phenyl-3-oxo-4-(diethylaminoethyl)piperazine, b0.03 112°, which with LiAlH4 gave 1-(4-chlorobenzyl)-2-phenyl-4-(diethylaminoethyl)piperazine, m. 103-4°. About 10 similar examples are given with their intermediates.

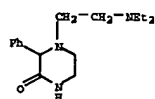
IT 26840-79-9F 26840-81-3F 26840-82-4P  
26840-86-8F 26840-87-9F 26840-92-6P  
26840-93-7F 26840-96-0F 26840-97-1P  
26921-23-3P  
EL: SYN (Synthetic preparation); PREP (Preparation)

RN 26840-79-9 CAPLUS  
CN Piperazinone, 4-[(4-chlorophenyl)methyl]-3-phenyl- (9CI) (CA INDEX NAME)

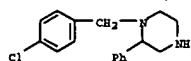


RN 26840-81-3 CAPLUS  
CN Piperazinone, 4-[(4-chlorophenyl)methyl]-3-phenyl- (8CI, 9CI) (CA INDEX NAME)

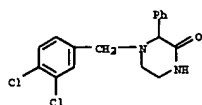
NAME)



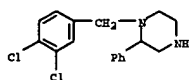
RN 26840-92-4 CAPLUS  
CN Piperazine, 1-[(4-chlorophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



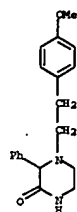
RN 26840-96-0 CAPLUS  
CN Piperazinone, 4-[(3,4-dichlorophenyl)methyl]-3-phenyl- (9CI) (CA INDEX NAME)



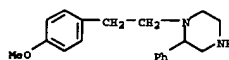
RN 26840-97-9 CAPLUS  
CN Piperazine, 1-[(3,4-dichlorophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



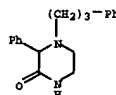
RN 26840-92-6 CAPLUS  
CN Piperazinone, 4-[2-(4-methoxyphenyl)ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 26840-93-7 CAPLUS  
CN Piperazine, 1-[2-(4-methoxyphenyl)ethyl]-2-phenyl- (9CI) (CA INDEX NAME)



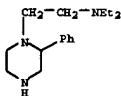
RN 26840-96-0 CAPLUS  
CN Piperazinone, 3-phenyl-4-[3-phenylpropyl]- (8CI, 9CI) (CA INDEX NAME)



RN 26840-97-1 CAPLUS  
CN Piperazine, 2-phenyl-1-(3-phenylpropyl)- (8CI, 9CI) (CA INDEX NAME)



RN 26921-23-3 CAPLUS  
CN 1-Piperazineethanamine, N,N-diethyl-2-phenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 98 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1969:512975 CAPLUS  
DOCUMENT NUMBER: 71:112975  
TITLE: Piperazine derivatives and their salts  
INVENTOR(S): Nitta, Yoshihiro; Ikeda, Yoshiaki; Furus, Toshiyuki;  
Shioya, Akito; Kanno, Shigeru; Shireki, Yasuyuki  
PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd.  
SOURCE: Jpn. Tokkyo Koho, 8 pp.  
CODEN: JAKKAD  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 44017388	B4	19690731	JP	19670629

GI For diagram(s), see printed CA Issue.

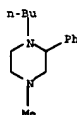
AB Manufacture of I, useful as coronary vasodilators and sedatives, is described. Thus, 9.3 g. ethylene oxide is introduced into 40 g. 1-phenyl-1-hydroxy-2-(benzylamino)ethane in 35 ml. MeOH to give 31.8 g. α-[N-benzyl(2-hydroxyethyl)aminomethyl]benzyl alc. (II), b1 191-3°; HCl salt m. 147-9°. II.HCl (15 g.) is heated with 65 ml. SOCl2 to give 10.5 g. 1-chloro-1-phenyl-2-[N-benzyl(2-chloroethyl)amino]ethane (III), b1 163-6°; picrate m. 195-8° (decomposition). III (2 g.) in 6 ml. EtOH is refluxed with 2.75 g. p-ClC6H4CH2N h2 to give 1.6 g. I (R1 = p-ClC6H4CH2, R2 = PhCH2), m. 102-3° (ligroins-C6H6). Similarly prepared are the following I (R1, R2, and m.p. given): p-MeC6H4CH2, PhCH2, 104-6°; 2-pyridyl, PhCH2, 86-8°; 5,2-Me(MeO)C6H3, Me, 102-4°; p-ClC6H4-CH2, Me, 82-3°; 2-pyridyl, Me, 65-6°; p-methylbenzyl, Me, 64-6°; p-tolyl, Me, 85-7°; Bu, Me, - (HCl salt m. 235-7°); PhCH2, Me, 83-5°; Ph, Me, 51-2°; p-methylbenzyl, Et, - (HCl salt m. 183-5°); p-ClC6H4CH2, Et, - (HCl salt m. 233-5°); p-tolyl, Et, - (HCl salt m. 192-4°); 2-pyridyl, Et, 74-5°.

IT 23174-95-09 23174-96-35 23174-99-4P

23175-00-0P  
RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

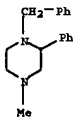
RN 23174-95-0 CAPLUS

CN Piperazine, 1-butyl-4-methyl-2-phenyl-, dihydrochloride (8CI, 9CI) (CA INDEX NAME)

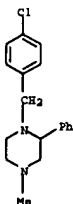


●2 HCl

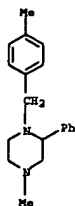
RN 23174-98-3 CAPLUS  
CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 23174-99-4 CAPLUS  
CN Piperazine, 1-[(4-chlorophenyl)methyl]-4-methyl-2-phenyl- (9CI) (CA INDEX NAME)



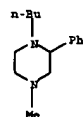
RN 23175-00-0 CAPLUS  
CN Piperazine, 4-methyl-1-(p-methylbenzyl)-2-phenyl- (8CI) (CA INDEX NAME)



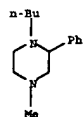
L7 ANSWER 99 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1969:501885 CAPLUS  
 DOCUMENT NUMBER: 71:101885  
 TITLE: Piperazine derivatives and their salts  
 INVENTOR(S): Nitta, Yoshihiro; Ikeda, Yoshiaki; Furue, Toshiyuki;  
 Shioya, Akitoshi; Kanno, Shigeru; Shiraki, Yasuyuki;  
 Chugai Pharmaceutical Co., Ltd.  
 PATENT ASSIGNEE(S): Jpn. Tokyo Koho, 7 pp.  
 SOURCE: CODEN: JAKXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 44018306	B4	19690811	JP	19670728
DE 1770743			DE	
FR 1571194			FR	
GB 1181322			GB	
US 3463548		19720000	US	

GI For diagram(s), see printed CA issue.  
 AB Manufacture of I, useful as a coronary vasodilator, is described. In an example, a mixture of 4.2 g. L-(+)-threo-1-(p-chlorobenzylamino)-1-phenyl-2-methylaminopropane, 2.75 g. 1,2-dibromoethane, and 2.4 g. NaOAc is heated at 120° 4 hrs., cooled, made strongly alkaline with 10% NaOH, and extracted with CH<sub>2</sub>Cl<sub>2</sub> to give 3.5 g. L-(+)-I (R<sub>1</sub> = p-chlorobenzyl, R<sub>2</sub> = R<sub>3</sub> = Me), b.p. 5-150-2°, m. 90-2° (petroleum ether). Similarly prepared are the following I (R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, b.p., and m.p. given): p-chlorobenzyl, H, Me, b.p. 179-81°, 82-3°; benzyl, H, Me, b.p. 149-51°, 83-5°; p-methylphenyl, H, Et, b.p. 137-40°, - (hydrochloride m. 192-4°); p-chlorobenzyl, H, benzyl, - 102-3°, 2-methoxy-5-methylphenyl, H, Me, b.p. 166-7°, 102-4°; Bu, H, Me, b.p. 124-5°, - (hydrochloride m. 235-7°); 2-pyridyl, H, Me, b.p. 155-7°, 65-6°; p-methylbenzyl, H, benzyl, - 104-6°.  
 IT 22287-90-7P 23174-95-0F 23174-98-3P  
 23174-99-4P 24160-12-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 22287-90-7 CAPLUS  
 CN Piperazine, 1-butyl-4-methyl-2-phenyl- (8CI, 9CI) (CA INDEX NAME)

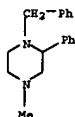


RN 23174-95-0 CAPLUS  
 CN Piperazine, 1-butyl-4-methyl-2-phenyl-, dihydrochloride (8CI, 9CI) (CA INDEX NAME)

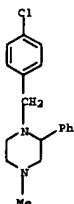


● 2 HCl

RN 23174-98-3 CAPLUS  
 CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

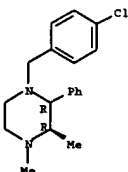


RN 23174-99-4 CAPLUS  
 CN Piperazine, 1-[(4-chlorophenyl)methyl]-4-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 24160-12-1 CAPLUS  
 CN Piperazine, 1-(p-chlorobenzyl)-3,4-dimethyl-2-phenyl-, trans-(+)- (8CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



attenuated the anesthetic properties of 3,3-dimethyl-2-oxopiperazine, 3-phenyl-2-oxopiperazine, and 3,3-diphenyl-2-oxopiperazine while their analgesic properties were retained.

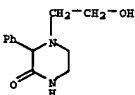
IT 5368-28-5F 22476-76-2F 23936-08-5P  
 23936-09-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 5368-28-5 CAPLUS  
 CN Piperazine, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



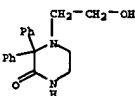
RN 22476-76-2 CAPLUS  
 CN Piperazinone, 3,3-diphenyl- (8CI, 9CI) (CA INDEX NAME)



RN 23936-08-5 CAPLUS  
 CN Piperazinone, 4-(2-hydroxyethyl)-3-phenyl- (9CI) (CA INDEX NAME)



RN 23936-09-6 CAPLUS  
 CN 2-Piperazinone, 4-(2-hydroxyethyl)-3,3-diphenyl- (8CI) (CA INDEX NAME)



L7 ANSWER 101 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1969:461336 CAPLUS  
 DOCUMENT NUMBER: 71:61336  
 TITLE: Piperazine compounds. I. Syntheses and pharmacological actions of 2-phenylpiperazine derivatives  
 AUTHOR(S): Nitta, Yoshihiro; Ikeda, Yoshiaki; Shiraki, Yasuyuki

L7 ANSWER 100 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1969:491427 CAPLUS  
 DOCUMENT NUMBER: 71:91427  
 TITLE: N-Memoalkylation of some 2-oxo- and 2,5-dioxopiperazines  
 AUTHOR(S): Sat., Mrs. A.; Podesta, Mrs. M.; Lattes, M. A.  
 CORPORATE SOURCE: Lab. Petrolechim., Nouv. Fac. Sci., Toulouse, Fr.  
 SOURCE: Chimica Therapeutica (1969), 4(3), 167-73  
 CODEN: CHTFBA; ISSN: 0009-4374  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 GI For diagram(s), see printed CA issue.  
 AB 3,3-Diphenyl-2-oxopiperazine was heated with ethylene oxide and water at 120° 16 hrs. to give 3,3-diphenyl-4-(2-hydroxyethyl)-2-oxopiperazine, m. 172°. 3-Phenyl-4-(2-hydroxyethyl)-2-oxopiperazine, m. 99°, was similarly prepared. Treatment of 3,3-dimethyl-2-oxopiperazine with ClCO<sub>2</sub>Et gave 3,3-dimethyl-4-ethoxycarbonyl-2-oxopiperazine, m. 150°, which on refluxing with Na and treatment with Ph-CH<sub>2</sub>Cl gave I (R = PhCH<sub>2</sub>), b.p. 180°, I (R = (CH<sub>2</sub>)<sub>2</sub>COAc), b.p. 150°, and I (R = Et), b.p. 120° were similarly prepared. Acid hydrolysis of I gave HO<sub>2</sub>CCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub>·2HCl (R and m.p. given): PhCH<sub>2</sub>, 230°, Et, 226°; HO(CH<sub>2</sub>)<sub>2</sub>, 190°. I (R = PhCH<sub>2</sub>) also gave 3,3-dimethyl-1-benzyl-2-oxopiperazine hydrochloride, m. 220°. Introduction of the hydroxyethyl group at the 4-position

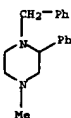
CORPORATE SOURCE: Res. Lab., Chugai Pharm. Co., Ltd., Tokyo, Japan  
SOURCE: Yakugaku Zasshi (1969), 89(5), 660-8  
CODEN: YKJZAJ; ISSN: 0031-6903  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese

GI For diagram(s), see printed CA issue.

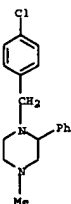
AB Various I are prepared as possible coronary vasodilators. Styrene oxide added with ice cooling to 3.5 moles aqueous R1NH2 and the mixture kept 5 days gave 36-44% PhCH(OH)CH2NH2 (II) (R1, b.p./mm., and m.p. given): Me, 132-4°/10, 75-6°; Et, 121-4°/1, 77-80°; PhCH2, -, 103-4°. Ethylene oxide (0.36 mole) passed through 0.3 mole II or di- or l-ephedrine in 30 ml. MeOH over 2 hrs. at 25 ± 3° and the mixture refluxed 1 hr. gave 63-84% PhCH(OH)CH(NHCH2CH2OH)R (R, R1, b.p., and m.p. HCl salt given): H, Me, 179-82°/5, -, H, Et, 142-4°/1, -, H, PhCH2, 191-3°/1, 147-9°, Me, Me, 136-9°/1, 134-5° (l-isomer, m. 113-14°, [α]20D -15.79°). Reaction at 80° reduced the yield. The hydrochloride heated with excess SOCl2 40 min. at 50° gave 60-5% PhCHClCH(NHCH2CH2Cl)R (III) (same data given): H, Me, 118-22°/1, 125-7°; H, Et, 110-13°/1, - (picrate m. 203-4°); H, PhCH2, 163-6°/1, - (picrate m. 195-8°); Me, Me, 135-7°/1, 150-1° [L-threo-isomer (IIa), m. 163-6°, [α]20D 86.32°, base, b1 115-16°, with PC15 in CHCl3]. R2NH2 (0.06 mole) added slowly to 0.02 mole III in 10 ml. EtOH caused boiling and the mixture refluxed 30 min. gave I (R, R1, R2, b.p./mm., m.p., and % yield given): H, Me, Bu, 124-5°/6, - (di-HCl salt semihydrate m. 235-7°); 70; H, Me, Ph, 129-41°/1.5, 51-2°, 64; H, Me, p-tolyl, 152-3°/1, 85-7°, 72; H, Me, 2,5-MeO(Me)C6H3, 166-7°/1, 102-4°, 69; H, Me, PhCH2, 153-4°/1.5, 83-5°, 66; H, Me, p-ClC6H4CH2, 179-81°/1, 82-3°, 69; H, Me, p-MeC6H4CH2, 143-4°/1.5, 64-5°, 69; H, Et, p-tolyl, 137-40°/1, - (HCl salt semihydrate m. 192-4°); 82; H, Et, p-ClC6H4CH2, 157-60°/1, - (HCl salt semihydrate m. 233-5°); 68; H, Et, p-MeC6H4CH2, 132-5°/1, - (HCl salt m. 183-5°); 66; H, PhCH2, p-ClC6H4CH2, -, 102-3°, 65; H, PhCH2, p-MeC6H4CH2, -, 104-6°, 69; Me, Me, 2,5-MeO(Me)C6H3, 145-7°/1.5, - (dipicrate m. 207-8°, difumarate m. 184-5°); 46; Me, Me, p-ClC6H4CH2 (Ia), 163-4°/1.5, 86-7°, 71 (62-5% yield with 1:1 molar reactants in the presence of K2CO3 or Et3N); Me, Me, p-MeC6H4CH2, 132-6°/1, 92-3°, 48. MONE2 (0.06 mole) in PhMe heated 1 hr. with 0.03 mole 2-aminopyridine and refluxed 5 hrs. with 0.03 mole II gave I (same data except R2 = 2-CSH4N): H, Me, 162-5°/1.8, 65-6°, 70; H, Et, 103-7°/1, 74-5°, 70; H, PhCH2, -, 86-8°, 62; Me, Me, 152-3°/1, - (dipicrate m. 125-8°); 43. Similarly, the following I (R = R1 = Me) were prepared with IIIa [R2, (4)23D (EtOH), b.p./mm., m.p., m.p. of dipicrate, and % yield given]: p-ClC6H4CH2 (Ib), 12-2°, 160-2°/0.5, 93-5-4.5°, -, 68; 2-CSH4N, 41.8°, 110-14°/0.5, -, 105-7°, 56. l-Ephedrine heated with PC15 and the product refluxed 5 hrs. with p-ClC6H4-CH2NH2 gave 70% PhCH(NHCH2C6H4Cl-p)CH(NHMe)Me, b0-5 155-7° (HCl salt, m. 240-1°), [α]20D 11.87°, converted (72%) to Ib by heating 4 hrs. at 120° with BzCH2CH2Br and NaOMe. Ia and Ib were >5 times as effective as aminophylline for increasing the coronary and femoral blood flow in dogs. The structure-activity relations were discussed.

IT 22287-90-7P 22287-93-0F 23174-95-0P  
23174-98-3P 23174-99-4F 23175-00-0P  
23175-14-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

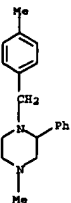
RN 22287-90-7 CAPLUS  
CN Piperazine, 1-butyl-4-methyl-2-phenyl- (8CI, 9CI) (CA INDEX NAME)



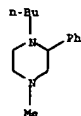
RN 23174-99-4 CAPLUS  
CN Piperazine, 1-[(4-chlorophenyl)methyl]-4-methyl-2-phenyl- (9CI) (CA INDEX NAME)



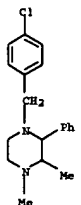
RN 23175-00-0 CAPLUS  
CN Piperazine, 4-methyl-1-[(p-methylbenzyl)-2-phenyl]- (8CI) (CA INDEX NAME)



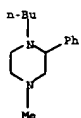
RN 23175-14-6 CAPLUS  
CN Piperazine, 1,2-dimethyl-4-(p-methylbenzyl)-3-phenyl- (9CI) (CA INDEX NAME)



RN 22287-93-0 CAPLUS  
CN Piperazine, 1-[(4-chlorophenyl)methyl]-3,4-dimethyl-2-phenyl- (9CI) (CA INDEX NAME)

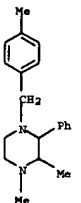


RN 23174-95-0 CAPLUS  
CN Piperazine, 1-butyl-4-methyl-2-phenyl-, dihydrochloride (8CI, 9CI) (CA INDEX NAME)



●2 HCl

RN 23174-98-3 CAPLUS  
CN Piperazine, 4-methyl-2-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L7 ANSWER 102 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1969:114546 CAPLUS  
DOCUMENT NUMBER: 69:114546  
TITLE: Structural effect of nitrogen-containing substances in the microdetermination of carbon and hydrogen with external absorption of nitrogen oxides  
AUTHOR(S): Mazzadro, Margherita; Farina, A.; Settini, Guido  
CORPORATE SOURCE: Ist. Super. Sanita, Rome, Italy  
SOURCE: Mikrokhoimika Acta (1968), (2), 332-43  
CODEN: MIACQA; ISSN: 0026-3672  
DOCUMENT TYPE: Journal  
LANGUAGE: German

GI For diagram(s), see printed CA issue.

AB A series of succinodinitrile derive. were prepared for studies of C- and H-dets. in the presence of M. Thus, NCCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub> (I) (R = H, R' = R'' = Me or Ph) were prepared by the method of R. Schwetick (1964); II [X = (CH<sub>2</sub>)<sub>2</sub>, R = H, R' = R'' = Me, Me.HCl, or Ph; X = (CH<sub>2</sub>)<sub>2</sub>, R = H, R' = R'' = Me; X = (CH<sub>2</sub>)<sub>2</sub>, R = Et, R' = R'' = Me; X = (CH<sub>2</sub>)<sub>2</sub>, R = H, R' = Me, R'' = Ph; X = (CH<sub>2</sub>)<sub>2</sub>, R = R' = Me, R'' = Ph; X = (CH<sub>2</sub>)<sub>2</sub>, (R,R' =) (CH<sub>2</sub>)<sub>4</sub>, R = H, Me, or Et; X = (CH<sub>2</sub>)<sub>3</sub>, R = H, R' = R'' = Me or (R,R' =) (CH<sub>2</sub>)<sub>4</sub>; X = (CH<sub>2</sub>)<sub>3</sub>NR(CN)R'C(CN)R''NR(CH<sub>2</sub>)<sub>3</sub>, R = H, R' = R'' = Me or (R,R' =) (CH<sub>2</sub>)<sub>4</sub>] and III by the method of O. Settini (1965); RR'N(CH<sub>2</sub>)<sub>2</sub>NR'R'' (IV) (R = H, x = 2, R' = CH<sub>2</sub>MeCN.HCl) by the method of V. Yasunaka (1962); IV [x = 2, R = H, R' = Me(CN)Et] by A. Ainley (1948); IV [x = 2, R = H, R' = CH(CN)Ph] by N. Schlesinger (1912). IV [x = 3, R = H, R' = CH(CN)Ph], m. 104-5°, and IV [x = 2, R = Me, R' = CH(CN)Ph], m. 145-6°, were also prepared by Schlesinger's method. 2,3-Butanedione, (20 millimoles) in 100 millimoles MeHSO<sub>3</sub> in 20 ml. H<sub>2</sub>O was stirred 1 hr. and treated with 40 millimoles KCN in 10 ml. H<sub>2</sub>O with cooling to give I (R = CH, R' = R'' = Me), m. 100-1°. I (R = CH, R' = Me, R'' = Ph), m. 102-3°, and I (R = CH, (R,R' =) (CH<sub>2</sub>)<sub>4</sub>), m. 113-15°, were similarly prepared I (R = CH, R' = R'' = Me) was treated with the stoichiometric amount of PhCHNH<sub>2</sub> to give I (R = NHCH<sub>2</sub>Ph, R' = R'' = Me), m. 130-1°. I (R = NHMe, R' = R'' = Me) m. 89-90°, and I (R = NHMe, (R,R' =) (CH<sub>2</sub>)<sub>4</sub>), m. 113-15°, were similarly prepared AcCH<sub>2</sub>Ac (0.1 mole), 0.1 mole KCN, and 0.05 mole H<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub> in 70 ml. H<sub>2</sub>O was kept at room temperature to give IV [x = 2, (RR' =) C(CN)Me(CH<sub>2</sub>)<sub>2</sub>C(CN)Me], m. 182-3°. The following IV [(R,R' =) C(CN)Me(CH<sub>2</sub>)<sub>2</sub>C(CN)Me] were similarly prepared (x and m.p. given): 3, 138-9°, 4, 152-3°, 5, 120-2°, 6, 115°. NC(CH<sub>2</sub>)<sub>2</sub>CN, H<sub>2</sub>NOC(CH<sub>2</sub>)<sub>2</sub>CN, V (R = H, R' = Me, R'' = R' = CONH<sub>2</sub>), V (R' = Ph, R'' = CN, R' = OH, R = Me or Et) were also used. Studies of the divergent behavior of the nitrogenous comds. upon C- and H-dets. with external absorption of the N oxides indicated that erroneously high E values were obtained for those comds. containing the group NOC(R<sub>2</sub>)C(R<sub>2</sub>)CN (VI), where the R groups can be the same

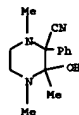
or different. However, for the compds. in which R of VI were Ph or OH, uniform R values were obtained. The compds. giving high R values can be analyzed for C and H by using a combustion method providing for the reduction of N oxides. The combustion tube consisted of a 60-cm. long, 9-mm. inner diameter quartz tube, containing an Ag wire and packed with 10 mm. CuO, 110 mm. reduced Cu, 70 mm. Ag wool, 40 mm. granulated Co3O4, and 120 mm. of a 1:2 Co3O4:Cu mixture. The layers were separated with quartz wool and heated to the following temps. for the combustion: reduced Cu, 550-600°; Ag wool, 480°; catalyst layer, 690-700°.

IT 18316-94-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and carbon-hydrogen microdetn. of)

EN 18316-94-4 CAPLUS

CN 2-Piperazinecarbonitrile, 3-hydroxy-1,4-trimethyl-2-phenyl- (8CI) (CA INDEX NAME)



L7 ANSWER 103 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1967:18688 CAPLUS

DOCUMENT NUMBER: 66:18688

TITLE: Radioprotective agents. IV. Piperazines and

pipazines related to phenylhydrazine

AUTHOR(S): Granger, Robert; Orzalesi, Henri; Robbe, Y.

CORPORATE SOURCE: Fac. Pharm., Montpellier, Fr.

SOURCE: Travaux de la Société de Pharmacie de Montpellier

(1965), 25(4), 313-17

DOCUMENT TYPE: Journal

LANGUAGE: French

GI For diagram(s), see printed CA Issue.

AB cf. preceding abstract. The title compds. were prepared Thus, 6.5 g.

2-amino-2-aminomethylpropane in 50 ml. absolute alc. containing 15 g. Et

oxalate

gave after the exothermic reaction subsided a precipitate of 65% I (R = R' =

Me), m. 204°. The following I were similarly prepared (R, R', & yield,

and m.p. given): Me, Ph, 76, 214°; Et, Ph (III), 73, 243-4°;

(RR' =) (CH2)4, 50, 246-8°; (RR' =) (CH2)5 (III), 67,

226-7°; (RR' =) (CH2)6, 71, 207-8°. LiAlH4 reduction of I gave

the corresponding piperazine. Thus was prepared from II 29%

2-phenyl-2-methylpiperazine, b.p. 190°, and from III 30%

2-phenyl-2-methylpiperazine, b.p. 110°.

13157-36-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

EN 13157-36-3 CAPLUS

CN Piperazine, 2-methyl-2-phenyl- (8CI, 9CI) (CA INDEX NAME)



EN 5368-20-7 CAPLUS

CN 2-Piperazinone, 4-methyl-3-phenyl- (7CI, 8CI) (CA INDEX NAME)



EN 5368-22-9 CAPLUS

CN 2-Piperazinone, 3-phenyl-4-propyl- (7CI, 8CI) (CA INDEX NAME)



EN 5368-23-0 CAPLUS

CN Piperazinone, 3-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



EN 5368-24-1 CAPLUS

CN 2-Piperazinone, 4-phenethyl-3-phenyl- (7CI, 8CI) (CA INDEX NAME)



EN 5368-26-5 CAPLUS

CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 104 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1966:59898 CAPLUS

DOCUMENT NUMBER: 64:59898

ORIGINAL REFERENCE NO.: 64:11209a-c

TITLE: Synthesis of pyridazine derivatives. V. Syntheses of

10H-pyridasino[3,2-b]quinazolin-10-one and its

derivatives. 2

AUTHOR(S): Yanai, Mitsuji; Kinoshita, Toshio; Nakashima, Shigeo

CORPORATE SOURCE: Univ. Nagasaki, Japan

SOURCE: Yakugaku Zasshi (1966), 86(1), 69-71

CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB cf. CA 63, 5638c. 4-Oxo-3,4-dihydro-2-quinazolinopropionitrile (0.1 g.)

is refluxed for 9 hrs. in 5 ml. concentrated HCl to give 40 mg.

4-oxo-3,4-dihydroquinazoline-2-propionic acid (I), m. 232-3°

(decomposition) (Me2CO). 2-Methyl-4-(3H)quinazolinone (10 g.) is boiled with 10

g. CCl3CHO and 25 ml. pyridine for 2 hrs. to give 13.5 g.

2-(3-trichloro-2-hydroxypropyl)-4(3H)-quinazolinone (II), m. 203-4°

(MeOH). A mixture of 3 g. II and 3 g. KOH dissolved in a small amount of H2O

is boiled for 15 min. with 120 ml. MeOH to give 0.15 g.

4-oxo-3,4-dihydro-2-quinazolinacrylic acid (III), m. 263.5-4.5°

(decomposition) (dilute EtOH). III (0.2 g.) in 150 ml. MeOH is subjected to

catalytic reduction using 15% Pd-C to give 72 mg. I. The same catalytic

reduction

in the presence of NH4OH gives the Me ester of I, m. 183.5-5°.

Heating 0.73 g. anthranilic acid with 0.5 g. 3-cyanopropionamide at

120° for 10 hrs. gives 20 mg. 2,2'-ethylenedi-4(3H)-quinazolinone,

m. >305° (MeOH).

IT 5271-27-2, Piperazine, 1-methyl-3-phenyl- 5271-28-3,

Piperazine, 1-methyl-2-phenyl- 5368-20-7, 2-Piperazinone,

4-methyl-3-phenyl- 5368-22-9, 2-Piperazinone, 3-phenyl-4-propyl-

5368-23-0, 2-Piperazinone, 4-benzyl-3-phenyl- 5368-24-1,

2-Piperazinone, 4-phenethyl-3-phenyl- 5368-26-5, 2-Piperazinone,

3-phenyl-

(preparation of)

EN 5271-27-2 CAPLUS

CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



EN 5271-28-3 CAPLUS

CN Piperazine, 1-methyl-2-phenyl- (7CI, 8CI) (CA INDEX NAME)



L7 ANSWER 105 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1966:59897 CAPLUS

DOCUMENT NUMBER: 64:59897

ORIGINAL REFERENCE NO.: 64:11208g-h,11209a

TITLE: Derivatives of piperazine. XXXV. Synthesis of

2-phenylpiperazine and some derivatives

AUTHOR(S): Roderick, William R.; Platte, Howard J.; Pollard, C.

CORPORATE SOURCE: Univ. of Florida, Gainesville

SOURCE: Journal of Medicinal Chemistry (1966), 9(2), 181-5

CODEN: JMCMAE; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 64:59897

AB cf. CA 54, 24761b. Three methods for the synthesis of 2-phenylpiperazine

(I), two of them new, were investigated. One method concerned the

condensation of ethyl α-bromophenylacetate with ethylenediamine to

form 3-oxo-2-phenylpiperazine followed by hydride reduction to I. This

method was superior to the condensation of styrene oxide with

ethylenediamine, previously employed. The 2nd method involved

condensation of Et glycinate, cyanide, and BzEt to ethyl

N-(α-cyanobenzyl)glycinate, which was hydrolyzed to the amido ester.

The latter was cyclized by NaH to 3,5-dioxo-2-phenylpiperazine which was

reduced to I. The 1-alkyl deriva. of I were obtained unambiguously by

alkylation of 3-oxo-2-phenylpiperazine followed by hydride reduction. The

4-alkyl and 1,4-dialkyl deriva. were prepared by alkylation of I.

IT 5271-26-1, Piperazine, 2-phenyl-

(deriva., preparation and pharmacological effects of)

EN 5271-26-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT 5271-27-2, Piperazine, 1-methyl-3-phenyl- 5271-28-3,

Piperazine, 1-methyl-2-phenyl- 5271-29-4, Piperazine,

1,4-dimethyl-2-phenyl- 5271-31-8, Piperazine, 1-ethyl-2-phenyl-

5368-21-8, 2-Piperazinone, 4-ethyl-3-phenyl- 5368-22-9,

2-Piperazinone, 3-phenyl-4-propyl- 5368-23-0, 2-Piperazinone,

4-benzyl-3-phenyl- 5368-24-1, 2-Piperazinone,

4-phenethyl-3-phenyl- 5368-26-5, 2-Piperazinone, 3-phenyl-

5368-30-9, Piperazine, 2-phenyl-1-propyl- 5368-33-2,

Piperazine, 1-benzyl-2-phenyl-

(preparation of)

EN 5271-27-2 CAPLUS

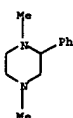
CN Piperazine, 1-methyl-3-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 5271-28-3 CAPLUS  
CN Piperazine, 1-methyl-2-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 5271-29-4 CAPLUS  
CN Piperazine, 1,4-dimethyl-2-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 5271-31-8 CAPLUS  
CN Piperazine, 1-ethyl-2-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 5368-21-8 CAPLUS  
CN 2-Piperazinone, 4-ethyl-3-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 5368-22-9 CAPLUS



L7 ANSWER 106 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1963:441714 CAPLUS  
DOCUMENT NUMBER: 59:41714  
ORIGINAL REFERENCE NO.: 59:7527h, 7528a-b  
TITLE: Synthesis of adenine-8-C14  
AUTHOR(S): Fel'dman, I. Kh.; Zlobina, V. I.  
SOURCE: Mekhnye Biol. Aktivn. Veshchestva, Sb. Statei (1962) 53-9  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
GI For diagram(s), see printed CA issue.  
AB Di-Et malonate (155 ml.) was mixed with 465 ml. concentrated NH<sub>3</sub> (22-23%), the mixture shaken for 40-45 min. until a transparent homogeneous liquid formed, and kept overnight to give 78.5% H<sub>2</sub>C(CO<sub>2</sub>H)<sub>2</sub> (I). By known methods, I was treated with H<sub>2</sub>NCHO and NaOEt to give, after acidification with HCl, 53.7% 4,6-dihydroxypyrimidine, decompose but does not melt above 300°, which gave, with HNO<sub>3</sub>, 76.5% the 5-NO<sub>2</sub> derivative, decompose but does not melt above 300°. Treatment of this with POCl<sub>3</sub> and Me<sub>2</sub>C<sub>6</sub>H<sub>4</sub> gave 86% 4,6-dichloro-5-nitropyrimidine, m. 102-4°, converted with NH<sub>3</sub> to 97% the 4,6-diamino analog, and then reduced with Fe and HCl to 82% 4,5,6-triaminopyrimidine (II), m. 252-3°. II and (H<sub>2</sub>N)<sub>2</sub>C<sub>14</sub>S gave 60% Chloedamine-8-C14 (III), which with H<sub>2</sub>O<sub>2</sub> gave 81% adenine-8-C14 sulfate, which treated with H<sub>2</sub>S gave the free base, m. 358-60° (decomposition).  
IT 5271-26-1, Piperazine, 2-phenyl- (synthesis of)  
RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

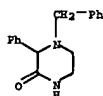


L7 ANSWER 107 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1963:441713 CAPLUS  
DOCUMENT NUMBER: 59:41713  
ORIGINAL REFERENCE NO.: 59:7527h  
TITLE: The synthesis of 2-phenylpiperazine and some derivatives  
AUTHOR(S): Platte, Howard Jean  
CORPORATE SOURCE: Univ. of Florida, Gainesville  
SOURCE: (1963) 59 pp. Avail.: Univ. Microfilms (Ann Arbor, Mich.), Order No. 62-6545  
From: Dissertation Abstr. 23, 3128  
DOCUMENT TYPE: Dissertation  
LANGUAGE: Unavailable  
AB Unavailable  
IT 5271-26-1, Piperazine, 2-phenyl- (synthesis of)

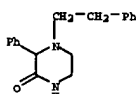
CN 2-Piperazinone, 3-phenyl-4-propyl- (7CI, 8CI) (CA INDEX NAME)



RN 5368-23-0 CAPLUS  
CN Piperazinone, 3-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 5368-24-1 CAPLUS  
CN 2-Piperazinone, 4-phenethyl-3-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 5368-28-5 CAPLUS  
CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



RN 5368-30-9 CAPLUS  
CN Piperazine, 2-phenyl-1-propyl- (7CI, 8CI) (CA INDEX NAME)



RN 5368-33-2 CAPLUS  
CN Piperazine, 2-phenyl-1-(phenylethyl)- (9CI) (CA INDEX NAME)

RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 108 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1963:441712 CAPLUS  
DOCUMENT NUMBER: 59:41712  
ORIGINAL REFERENCE NO.: 59:7527e-h  
TITLE: Nucleophilic substitution of  $\alpha$ -bromo diesters  
AUTHOR(S): Gelin, Rene; Gelin, Suzanne  
CORPORATE SOURCE: Inst. Natl. Sci. Appl., Villeurbanne, Fr.  
SOURCE: Compt. Rend. (1963), 256, 3705-8  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
OTHER SOURCE(S): CASREACT 59:41712  
AB By treatment of  $\alpha$ -bromodiethers with NaNO<sub>2</sub> the following corresponding EtO<sub>2</sub>CCH(NO<sub>2</sub>)CH<sub>2</sub>NO<sub>2</sub>Et were prepared (n, b.p./mm., n<sub>D</sub>25, d<sub>25</sub> given): 1, 116°/1 and 132-3°/3, -, - (an appreciable amount di-Et maleate was also obtained in this case); 2, 115°/0.5, 1.441, 1.1667; 3, 134°/0.7 and 140°/1, -, -, Na (23 g.) in 250 ml. absolute EtOH treated with 1 mole appropriate phenol in 100 ml. EtOH, the solution treated during 15 min. with 1 mole appropriate  $\alpha$ -bromo diester, heated 3 hrs. on a boiling H<sub>2</sub>O bath, concentrated, treated with H<sub>2</sub>O, and the organic layer washed with 10% aqueous Na<sub>2</sub>CO<sub>3</sub>, dried, and distilled gave  $\alpha$ -aryloxydiesters. In this manner were prepared the following RO<sub>2</sub>CCH(OC<sub>6</sub>H<sub>4</sub>R<sub>1</sub>)(CH<sub>2</sub>)<sub>2</sub>NO<sub>2</sub>Et (R, R<sub>1</sub>, n, b.p./mm., n<sub>D</sub>25, d<sub>25</sub>, m.p. corresponding diacid given): Et, H, 2, 160°/1.5, 1.488, 1.1101, 105°; Et, o-Me, 2, 149°/0.5, 1.488, 1.0879, 139°; Et, H, 3 (II), 155°/0.5 and 169°/0°/1, 1.486, 1.0489, 140°. Similar treatment of EtO<sub>2</sub>CCHBrCH<sub>2</sub>CO<sub>2</sub>Et with PhONa solution resulted only in the loss of HBr. Dieckmann condensation of I gave 62% 3-phenoxo-2-oxocyclopentanecarboxylate (II), b.p. 163-4°, n<sub>D</sub>25 1.531, d<sub>25</sub> 1.1592; semicarbazone m. 145°. II saponified and the resulting acid decarboxylated gave 60% 2-phenoxycyclopentanone (III), b.p. 128-30°, semicarbazone m. 205°. Treatment of EtO<sub>2</sub>CCH(OC<sub>6</sub>H<sub>4</sub>R<sub>1</sub>)(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H with BaO at 280° gave a poor yield of III. Treatment of 0.52 mole pyrrolidine in C<sub>6</sub>H<sub>6</sub> with 0.25 mole appropriate  $\alpha$ -bromo diester gave the following EtO<sub>2</sub>CCH(R)(CH<sub>2</sub>)<sub>2</sub>NO<sub>2</sub>Et (IV) (R = pyrrolidino) (n,  $\eta$  yield, b.p./mm., n<sub>D</sub>25, d<sub>25</sub> given): 1, 75, 116°/1, 1.453, 1.0523; 2, 42, 128°/1, 1.455, 1.0425; 3, 62, 139°/1, 1.4566, 1.0309. Derivs. of IV in which R was piperidine, morpholine, piperazine, and Et<sub>2</sub>NH were also prepared, known compds. being obtained.

IT 5271-26-1, Piperazine, 2-phenyl- (synthesis of)  
RN 5271-26-1 CAPLUS  
CN Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 109 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1963:59797 CAPLUS  
DOCUMENT NUMBER: 58:59797  
ORIGINAL REFERENCE NO.: 58:10214a-c  
TITLE: 3-Substituted 2-oxopiperazines  
INVENTOR(S): Kawahara, Shigemi; Kawakami, Hideyo  
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd.  
SOURCE: 2 pp.  
DOCUMENT TYPE: Patent  
LANGUAGE: Unavailable  
PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	JP 37004540		19620614	JP	19590508

GI For diagram(s), see printed CA Issue.  
AB Into a mixture of 40 g. ethylenediamine and 200 cc. C<sub>6</sub>H<sub>6</sub> is dropped a solution of 40 g. Me  $\alpha$ -bromophenylacetate in 100 cc. C<sub>6</sub>H<sub>6</sub> during 2.5 hrs. and the mixture is refluxed 2 hrs. and concentrated to half volume; ethanolic KOH solution is added, the mixture filtered, and the filtrate concentrated to give 13 g. 3-phenyl-2-oxopiperazine (I, R = Ph, R<sub>1</sub> = H), m. 141-2° (Me<sub>2</sub>CO) (hydride m. 216.5-17.5°). Similarly prepared are the following I (R, R<sub>1</sub>, m.p. and m.p. HI salt given): cyclohexyl, H, 149-50°, 211-12°, Ph, Ph, 156-7°, 218-19°, p-chlorophenyl, H, 134-5°, ... These are analgesics and anti-spasmodics.  
IT 5368-28-5, 2-Piperazinone, 3-phenyl- 22476-76-2, 2-Piperazinone, 3,3-diphenyl- 93690-93-8, 2-Piperazinone, 3-phenyl-, hydride (preparation of)  
RN 5368-28-5 CAPLUS  
CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



RN 22476-76-2 CAPLUS  
CN Piperazinone, 3,3-diphenyl- (8CI, 9CI) (CA INDEX NAME)



RN 93690-93-8 CAPLUS  
CN 2-Piperazinone, 3-phenyl-, hydride (7CI) (CA INDEX NAME)

CN Piperazinone, 3,3-diphenyl- (8CI, 9CI) (CA INDEX NAME)



RN 93648-84-1 CAPLUS  
CN 2-Piperazinone, 4-methyl-3,3-diphenyl- (7CI) (CA INDEX NAME)



RN 94033-08-6 CAPLUS  
CN 2-Piperazinone, 4-methyl-3-phenyl-, hydride (7CI) (CA INDEX NAME)



• HI

RN 857192-21-3 CAPLUS  
CN 2-Piperazinone, 4-methyl-3,3-diphenyl-, hydrochloride (7CI) (CA INDEX NAME)



• HC1

RN 857192-34-8 CAPLUS  
CN 2-Piperazinone, 3,3-diphenyl-, hydrochloride (7CI) (CA INDEX NAME)



• HI

L7 ANSWER 110 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1963:40295 CAPLUS  
DOCUMENT NUMBER: 58:40295  
ORIGINAL REFERENCE NO.: 58:6921c-e  
TITLE:  $\alpha$ -Aminophenylacetic acid derivatives having antispasmodic activity and their related compounds. III. Synthesis of 3-substituted-2-piperazinones and their 4-methyl derivatives  
AUTHOR(S): Kawahara, Shi-gemi; Kawakami, Hideyo  
CORPORATE SOURCE: Yamanouchi Pharm. Co., Tokyo  
SOURCE: Yakugaku Zasshi (1962), 82, 909-12  
CODEN: YKZZAJ; ISSN: 0031-6903  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
GI For diagram(s), see printed CA Issue.  
AB cf. CA 56, 4658a. (HZNCH2)2 (22.5 g.) in 40 ml. C<sub>6</sub>H<sub>6</sub>, treated dropwise with 20 g. p-BrC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>Et in 40 ml. C<sub>6</sub>H<sub>6</sub>, the mixture refluxed 2 hrs., the solution concentrated, KOH-EtOH added, the KBr filtered off, and the filtrate concentrated gave 41% I (R = p-BrC<sub>6</sub>H<sub>4</sub>, R<sub>1</sub> = H), m. 168-9° (HCl salt, m. 233-5°). Similarly were prepared I (R, R<sub>1</sub>, % yield, b.p./mm. or m.p., and m.p. of HCl salt given): Me, H, 41.7, 135-7°/3, 202-3°, Et, H, 56.5, 59-60°, 168-9°, Bu, H, 41.7, 135-7°/3, 202-3°, C<sub>6</sub>H<sub>11</sub>, H, 49.3, 149-50°, 233-4°, Ph, H, 44.4, 141-2°, --, p-ClC<sub>6</sub>H<sub>4</sub>, H, 45, 134-5°, 210-17°, Ph, Ph, 45.4, 158-9°, 241-2°. I (R = Et, R<sub>1</sub> = Ph) (1 g.), 1.5 g. MeI, and 3 ml. EtOH refluxed 5 hrs. and the product filtered gave II (R = Et, R<sub>1</sub> = Ph), m. 227-9°. Similarly were prepared II (R, R<sub>1</sub>, and m.p. of HCl salt given): Me, H, 239-40°, C<sub>6</sub>H<sub>11</sub>, H, 211-12°, Ph, H, 216-17°, p-BrC<sub>6</sub>H<sub>4</sub>, H, 228-9°. These compds. showed no antispasmodic action.  
IT 5368-28-5, 2-Piperazinone, 3-phenyl- 22476-76-2, 2-Piperazinone, 3,3-diphenyl- 93648-84-1, 2-Piperazinone, 4-methyl-3,3-diphenyl- 94033-08-6, 2-Piperazinone, 4-methyl-3-phenyl-, hydride 857192-21-3, 2-Piperazinone, 4-methyl-3,3-diphenyl-, hydrochloride 857192-34-8, 2-Piperazinone, 3,3-diphenyl-, hydrochloride (preparation of)  
RN 5368-28-5 CAPLUS  
CN Piperazinone, 3-phenyl- (8CI, 9CI) (CA INDEX NAME)



RN 22476-76-2 CAPLUS



• HCl

L7 ANSWER 111 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1962:2438 CAPLUS  
DOCUMENT NUMBER: 56:2438  
ORIGINAL REFERENCE NO.: 56:462a-g  
TITLE: Substituted piperazinone  
INVENTOR(S): Melone, Gaetano; Vecchi, Alberto; Maffii, Giulio  
PATENT ASSIGNEE(S): Lepetit S.p.A.  
DOCUMENT TYPE: Patent  
LANGUAGE: Unavailable  
PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB	870888		19610621	GB	

AB 3-Phenyl-3-methyl-2-piperazinone (I) is effective as an anticonvulsive agent. I, m. 165-7°, is obtained in 59% yield by heating at 160° 20 min. 17 g. Et  $\alpha$ -phenyl- $\alpha$ -chloropropionate (II) and 36 cc. anhydrous (CH<sub>2</sub>)<sub>2</sub>(NH<sub>2</sub>)<sub>2</sub>, cooling, adding 200 cc. anhydrous EtOH, evaporating to dryness in vacuo, adding 50 cc. H<sub>2</sub>O, and recrystg. from light petroleum. II is obtained in 81% yield, b.p. 117-19°, by mixing 120 g. acroleic acid and 280 cc. SOCl<sub>2</sub>, letting stand 36 hrs., distilling the excess SOCl<sub>2</sub> at room temperature, distilling the residual oil at 107-9°/15 mm., adding 700 cc. anhydrous EtOH, letting stand 3 hrs., evaporating to dryness, and distilling at 117-19°.  
IT 86311-16-2, 2-Piperazinone, 3-methyl-3-phenyl- (preparation of)  
RN 86311-16-2 CAPLUS  
CN Piperazinone, 3-methyl-3-phenyl- (9CI) (CA INDEX NAME)



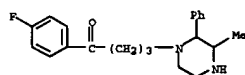
L7 ANSWER 112 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1961:28013 CAPLUS  
DOCUMENT NUMBER: 55:28013  
ORIGINAL REFERENCE NO.: 55:5549c-1, 5550a-1, 5551a-g  
TITLE: 1-Arylalkyl-4-arylpiperazines  
INVENTOR(S): Janssen, Paul A. J.  
DOCUMENT TYPE: Patent  
LANGUAGE: Unavailable  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
DE 589092 19600415 DE  
BE 1185615 DE  
GB 872352 GB  
AB 1-[γ-(4-benzoylpropyl)-4-phenylpiperazine, m. 89-90° (4:5 iso-PrOH-Et<sub>2</sub>O), was prepared by reaction of 7.5 g. chlorobutylphenol and 13.4 g. 1-phenylpiperazine 6 hrs. at room temperature and 4 hrs. at 105-10°, after cooling, 200 g. Et<sub>2</sub>O was added, the solution dried and evaporated, the residue dissolved in hot 4:1 70% EtOH-Et<sub>2</sub>O, and precipitated on cooling. The following 1-(aryalkyl)piperazines (1-arylalkyl = γ-benzoylpropyl) were thus prep'd (4-aryl group and m.p. given): 3-fluorophenyl, 80.2-81.6° (iso-PrOH); 3-chlorophenyl, 88-90°; 4-chlorophenyl, 127-8° (10:1 petr. ether-EtOH); 2-tolyl (HCl salt), 205-7° (5:4:3 iso-PrOH-MeOH-acetone); 3-tolyl, 78-9° (13:1 petr. ether-EtOH); 4-tolyl, 87.5-8.5° (iso-PrOH-Et<sub>2</sub>O); 2,5-xyllyl (HCl salt), 229-30°; 2-anisyl (di-HCl salt), 207.5-9.5° (iso-PrOH); 4-anisyl, 85-6° (iso-PrOH); 2-pyridyl, 63-4.8°; 4-methyl-2-pyridyl, 72-5.8°; 4-methyl-2-pyridyl, 65.5-6.5°; 3-cyano-2-pyridyl, 45.5-7°; 5-methyl-2-pyridyl, 71.5-3°; 2-pyrimidyl, 78-9°; 4-methyl-2-pyrimidyl, 62.4-3.2°; 4,6-dimethyl-2-pyrimidyl, 97.4-8°. The following 1-(5-benzoylbutyl)piperazines: Ph (di-HCl salt), 209-12° (8:8:1 acetone-iso-PrOH-MeOH); 3-tolyl (di-HCl salt), 191.5-2.5°; 2-pyridyl (di-HCl salt), 206.5-7.5°; 1-[γ-(4-fluorobenzoylpropyl)piperazines: Ph, 104-6° (iso-PrOH); 3-fluorophenyl (di-HCl salt), 198-200°; 4-fluorophenyl (di-HCl salt), 199.5-201.1°; 4-fluorophenyl (HCl salt), 180.2-1.6° (acetone-iso-PrOH); 2-chlorophenyl (HCl salt), 211-14° (iso-PrOH); 3-chlorophenyl (HCl salt), 197.8-9.5° (acetone-MeOH); 4-chlorophenyl, 96-8° (40:3 petr. ether-EtOH); 2-tolyl (HCl salt), 219-41° (decomposition); 3-tolyl (di-HCl salt), 210-12° (decomposition); 4-tolyl, 99-101° (iso-PrOH-Et<sub>2</sub>O); 2,5-xyllyl (di-HCl salt), 237.5-9.5°; 2-anisyl, 67.5-8.5° (iso-PrOH) (di-HCl salt m. 205.5-5.5°); 4-anisyl, 104.6-5.5° (iso-PrOH); 5-methyl-2-pyridyl, 92-3°; 4-methyl-2-pyrimidyl (di-HCl salt), 215-20°; 1-[γ-(4-chlorobenzoylpropyl)piperazines: Ph, 113.5-14.5°; 3-chlorophenyl, 86-8°; 3-tolyl, 99.6-10.4°; 4-tolyl, 129.5-20.5°; 4-anisyl, 126.6-7.8°; 4-fluorophenyl (HCl salt), 207-5°; 4-chlorophenyl, 127-0.5°; 2-pyridyl, 82.5-4.4°; 1-[γ-(4-methylbenzoylpropyl)piperazines: Ph, 103-4.8°; 2-chlorophenyl, 106-7°; 3-chlorophenyl, 124.5-5.5°; 4-chlorophenyl, 134.5-6°; 3-tolyl, 87-0.5°; 4-tolyl, m. 117.2-19.2°; 2-pyridyl, 92-3°; 4-anisyl, 123-3.4°; 1-[γ-(2,5-dimethylbenzoylpropyl)piperazines: Ph (HCl salt), 179.5-80.5°; 1-[γ-(4-anisoylpropyl)piperazines: 3-fluorophenyl, m. 111-13°; 2-chlorophenyl, 73.5-3.8°; 3-iodophenyl, -; 3-chlorophenyl, 101.6-2.4°; 4-chlorophenyl, 128.6-30°; 2-tolyl (HCl salt), 239.5-40.5°; 3-tolyl, 105-6°; 4-tolyl, 126.6-7.6°; 2,5-xyllyl (HCl salt), 225-6°; 2-anisyl (di-HCl salt), 197-8.2°; 4-anisyl, 125.6-7.4°; 1-[γ-(2,4-dimethoxybenzoylpropyl)piperazines: Ph (di-HCl salt), 195-6°; 2-tolyl (HCl salt), 177-9.2°; 2-anisyl (HCl salt), 214-15°; 2-pyridyl, 84.5-5.5°; 4-methyl-2-pyridyl, 79-80.8°; 1-[γ-(3,4-dimethoxybenzoylpropyl)piperazines: Ph, 101-3.5°; 2-pyridyl, 104.5-4.9°; 4-methyl-2-pyridyl, 85.4-6.5°; 1-[γ-(2,5-dimethoxybenzoylpropyl)piperazines: Ph (di-HCl salt), 179-80°; 1-[γ-(2,4,6-trimethoxybenzoylpropyl)piperazines: Ph, 113-16.2°; 1-[γ-(4-ethoxybenzoylpropyl)piperazines: Ph, 125.2-6.8°; 3-tolyl, 113.4-13.8°; 1-(β-Benzylyl-γ-benzoylpropyl)piperazines: Ph (di-HCl salt), 219.5-21.5°; 3-tolyl, (HCl salt), 228-32.5°; 1-[γ-(4-anisoylpropyl) compds.: benzoyl (HCl salt), 200.2-3.2°; 4-fluorobenzoyl, 65.2-6.2°; 2-anisoyl, 97-8.2°; 2,6-dimethoxybenzoyl (oxalate), 201.5-1.8°; 1-[γ-(2-thenoylpropyl) compds.: 4-fluorobenzoyl, 82.5-3.5°; 4-nicotinoyl, 64.6-5.8°; 2-thenoyl, 85.6-7.4°; 1-Phenyl-4-(4-phenylpiperazinyl)-1-butanol-2-HCl, m. 198-200°, was prepared by reaction of 8.5 g. 1-[γ-(benzoylpropyl)-4-phenylpiperazine and 0.25 g. NaH<sub>2</sub> in 160 cc. absolute EtOH at 45-50°; decomposition with 2H<sub>2</sub>SO<sub>4</sub>; the distillation residue was treated with aqueous alkali solution, extracted with Et<sub>2</sub>O, and treated with dry HCl. Following 1-phenyl-4-(R-substituted-piperazinyl)-1-butanol-2-HCl were similarly prepared (R given): 4-(3-tolyl), 83.5-4.5°; 4-(4-tolyl), 90.2-1.8°; 4-(3-fluorophenyl), 70-1.5°; 4-(3-chlorophenyl), 99-9.9°; 4-(4-chlorophenyl), 105-6°; 4-(4-anisyl), 91.5-2.6°; 4-(4-methyl-2-pyridyl), 78.5-80°; 4-(2-pyridyl), 113.8-14.8°; 1-(4-tolyl) analogs: 4-Ph, 104.5-6°; 4-(4-tolyl), 105-6°; 4-(4-anisyl), 84-5°; 4-(2-pyridyl), 119.2-19.8°; 1-(2,5-Xyllyl) analogs: 4-Ph, 92.8-3.8°; 1-(4-fluorophenyl) analogs: 4-Ph, 85.5-7.5° (HCl salt m. 143.5-6.5°); 4-(3-chlorophenyl), 100-1.8°; 4-(4-chlorophenyl), 112.5-13.8°; 4-(2-anisyl), 105-6°; 4-(4-tolyl), 93-5°; 4-(2-pyridyl), 104-5°; 4-(4-chlorophenyl) analogs: 4-Ph, 93.5-5°; 4-(3-chlorophenyl), 94-5°; 4-(4-chlorophenyl), 132-2°; 4-(3-tolyl), 93-4.5°; 1-(4-anisyl) analogs: 4-Ph, 104.2-7.2°; 4-(2-chlorophenyl), 106.8-8.4°; 4-(3-tolyl), 119.5-21.5°; 4-(4-tolyl), 109.5-10.2°; 1-(4-ethoxyphenyl) analogs: 4-Ph, 113-14.8°; 1-(2-thienyl) analogs: 4-Ph, 91.4-3°; 4-(3-tolyl), 76-8°; 4-(4-tolyl), 113-14°; 4-(3-fluorophenyl), 78-9°; 4-(4-chlorophenyl), 109.2-10°; 4-(2-chlorophenyl), 95.7-5°; 4-(3-chlorophenyl), 81.5°; 4-(2-pyridyl), 95-7°; 4-(2-pyrimidyl), 97.6-9.4°; 1-Phenyl-5-(4-phenylpiperazinyl)-1-pentanol, m. 111-12°, and 1-phenyl-5-(4-(3-tolyl)piperazinyl)-1-pentanol, m. 107-4-9.2° were also prepared 1-[γ-(4-anisoylpropyl)-4-(6-methyl-2-pyridyl)piperazine, m. 74-6°, was prepared by heating 8 hrs. at 110° 6.2 g. γ-chloro-4-methoxybutylphenol and 8.9 g. 1-(6-methyl-2-pyridyl)piperazine. 1-(γ-benzoylpropyl)-4-(6-methylthio-3-pyridinyl)piperazine, m. 124-5°, was prepared by heating in a sealed tube 48 hrs. at 140-50°, 14.0 g. 1-[γ-benzoylpropyl)piperazine, 5 g. 3-chloro-6-(methylthio)pyridazine, 120 g. toluene, and 0.01 g. KI. N-(4-Tolylsulfonyl)-N-(β-hydroxyethyl)-N-(β-hydroxypropyl)amine (II), m. 66.2-0.2° (iso-PrOH and petr. ether at -20°), was prepared by adding 190.5 g. 4-toluenesulfonyl chloride to 119 g. N-(β-hydroxyethyl)-N-(β-hydroxypropyl)amine and 54 g. Na<sub>2</sub>CO<sub>3</sub> in 450 g. H<sub>2</sub>O at 70°, heating 1 hr. at 95°, cooling, and extracting with Et<sub>2</sub>O. Reaction of 450 g. I and 690 g. SOCl<sub>2</sub> at 125° 1 hr., yielded N-(4-tolylsulfonyl)-N-(β-chloroethyl)-N-(β-chloropropyl)amine (III). Adding slowly 9.3 g. aniline in 15 cc. cyclohexanol to a hot mixture of 31 g. II, 32 g. Na<sub>2</sub>CO<sub>3</sub>, 0.1 g. KI, and 215 g. cyclohexanol, refluxing 48 hrs., cooling, filtering, adding C<sub>6</sub>H<sub>6</sub>, Et<sub>2</sub>O, H<sub>2</sub>O, and concentrated HCl precipitated 1-(4-tolylsulfonyl)-3-methyl-4-phenylpiperazine (HCl) (III), m. 214-20° (decomposition). Powdered 3-methyl-4-phenylpiperazine-2HBr, m. 193.4-9° (decomposition), was prepared by stirring at 30° 24 hrs. 93.5 g. III, 71.7 g. phenol, and 570 g. 30% HBr in AcOH, treating the product with Et<sub>2</sub>O, then boiling acetone. The free base in 4-methyl-2-pentanone was refluxed 22 hrs. with 11.2 g. γ-chloro-4-methoxybutylphenol, 12.4 g. Na<sub>2</sub>CO<sub>3</sub>, and 0.1 g. KI; the product was treated with active C, then with dry HCl in Et<sub>2</sub>O to yield 1-[γ-(4-fluorobenzoylpropyl)-3-methyl-4-phenylpiperazine-2HCl, m. 227-24.5° (decomposition). Following 1-substituted-3-methyl-4-substituted-piperazines were similarly prepared (1- and 4-substituents and

32.8-3.8° (petr. ether); 2-anisyl (di-HCl salt), 193-7°; 1-[γ-(4-iodobenzoylpropyl)piperazines: 5-methyl-2-pyridyl, -; 2-pyridyl, -; 4-methyl-2-pyrimidyl (di-HCl salt), -; 2-thiazolyl, -; 1-[γ-(4-methoxybenzoylpropyl)piperazines: 6-methyl-2-pyridyl, 74-6°; 4-methyl-2-pyridyl, 69.5-70.5°; 5-methyl-2-pyridyl, 84.6-6°; 3-cyano-2-pyridyl, 73.5-5.5°; 2-pyrimidyl, 83-3.5°; 2-thiazolyl (di-HCl salt), 122-4°; 4-methyl-2-pyrimidyl, 90°; 4,6-dimethyl-2-pyrimidyl, 71.8-4°; 2-(4-methylthiazolyl), 62.5-72° (di-HCl salt m. 187-201°); 2-(5-methyl-1,3,4-thiadiazolyl), 111.5-12.5°; 1-[γ-(2-thenoylpropyl)piperazines: 2-pyridyl, 70-1°; 5-methyl-2-pyridyl, 89.5-90.5°; 4-methyl-2-pyridyl, 65-6°; 6-methyl-2-pyridyl, 107.5-8.5°; 3-cyano-2-pyridyl, 71.5-2.5°; 2-pyrimidyl, 57.5-8.6°; 4-methyl-2-pyrimidyl, 52-3° (di-HCl salt m. 214.8-17°); 4,6-dimethyl-2-pyrimidyl, 64.5-5.6°; 2-thiazolyl, 52.2-4.6°; 2-(4-methylthiazolyl) (di-HCl salt), 163-6°; 2-(5-methyl-1,3,4-thiadiazolyl), 83.6-5.6°; Ph (HCl salt), 186-7°; 3-fluorophenyl, 68.2-70.2°; 2-chlorophenyl (HCl salt), 202.5-3°; 3-chlorophenyl, 103.6-4.6°; 4-chlorophenyl, 94.5-6.5°; 2-tolyl (HCl salt), 212-13°; 3-tolyl, 74-6°; 4-tolyl, 77.5-8.5°; 2,5-xyllyl (di-HCl salt), 214-15°; 2-anisyl (di-HCl salt), 197-201.8°; 4-anisyl, 69-70°; 1-[γ-(4-fluorobenzoylpropyl)piperazines: 4,6-dimethyl-2-pyrimidyl, 85.5-7.5°; 2-pyrimidyl, 111.6-12.8°; 2-thiazolyl, 74.5-6.5°; 2-(5-methylthiazolyl), 73-5.2°; 2-(5-methyl-1,3,4-thiadiazolyl), 105-6°; 2-(1,3,4-thiadiazolyl), 94.6-5.8°; 1-[γ-(γ-benzoylpropyl)piperazines: 2-thiazolyl, 61.5-4°; 2-(4-methylthiazolyl) (di-HCl salt), 186-8°; 2-(1,3,4-thiadiazolyl), 59-64°; 2-(5-methyl-1,3,4-thiadiazolyl), 98-100.2°; 1-(γ-benzoylpropyl)-4-(4-fluorophenyl)piperazine di-HCl salt, m. 214.5-17° (1:2:2 acetone-iso-PrOH-MeOH), was prepared by heating in a sealed tube 72 hrs. at 145-50° 9.1 g. γ-chlorobutylphenol, 23 g. 1-(4-fluorophenyl)piperazine, and 0.1 g. KI, extracting the cooled mixture with H<sub>2</sub>O and Et<sub>2</sub>O, and treating the dried organic layer with dry HCl; the base was liberated in aqueous alkaline solution, m. 104.5-5° (EtOH). 1-[γ-(4-anisoylpropyl)-4-phenylpiperazine, m. 126.6-7.5°, and the corresponding 4-fluorophenyl derivative, m. 121.2-1.8°, 1-[γ-(2-thenoylpropyl)-4-phenylpiperazine-2HCl, decomposed at 203-5°, and the 4-fluorophenyl analog, m. 62.5-3°, were similarly prepared. 1-[γ-(4-fluorobenzoylpropyl)-4-(3-methyl-2-pyridyl)piperazine-HCl, m. 212-20° (iso-PrOH), was prepared from 4.4 g. γ-chloro-4-fluorobutylphenol and 7.8 g. 1-(3-methyl-2-pyridyl)piperazine in 120 cc. C<sub>6</sub>H<sub>6</sub> in a sealed tube at 125° 24 hrs. The following derivs. were similarly prepared 1-[γ-(4-fluorobenzoylpropyl) compound (4-aryl and m.p. given): 4-methyl-2-pyridyl, 75.5-8.1°; 3-cyano-2-pyridyl, 71.5-3.5°; 6-chloro-3-pyridazinyl, 152-3.3°; 1-[γ-(4-methoxybenzoylpropyl) compound: 6-chloro-3-pyridazinyl, 176-6.8°; 1-[γ-(2-thenoylpropyl) compound: 6-chloro-3-pyridazinyl, 138-8.8°; 6-methoxy-3-pyridazinyl, 98.8-9.8°; 1-(γ-benzoylpropyl)-4-benzoylpiperazine, m. 85-6° (iso-PrOH), was prepared by heating a stirred mixture of 7 g. 1-(γ-benzoylpropyl)piperazine, 40 g. C<sub>6</sub>H<sub>6</sub>, 50 g. 10% NaOH solution, and (dropwise) 4.5 g. BzCl, and keeping the mixture at 70° 45-60 min. The following 1-(γ-benzoylpropyl) compds. were similarly prepared (same data): 4-fluorobenzoyl (HCl salt), 214.5-16.5°; 2-chlorobenzoyl (HCl salt), 216-17.5°; 3-chlorobenzoyl (HCl salt), 210.5-12.5°; 4-chlorobenzoyl, 98-9°; 3-trifluoromethylbenzoyl, 77.5-9°; 2-anisoyl (HCl salt), 140.8-3°; 2,6-dimethoxybenzoyl (oxalate), 187.4-8.2°; 182.1-4.8°; 3,4,5-trimethoxybenzoyl (oxalate), 187.4-8.2°; 5-(3-methyl-1,2,4-thiadiazolyl), 79-9°; 3-carboxamido-2-pyridyl, 112.6-14.2°; 1-[γ-(4-fluorobenzoylpropyl) compds.: benzoyl

m.p. given): γ-benzoylpropyl, Ph (di-HCl salt), 229-33° (4-(2-anisyl) analog (di-HCl salt) m. 212-15°); γ-(4-anisoylpropyl), Ph, 92-3.8° (4-(2-anisyl) analog (di-HCl salt) m. 199-200°); γ-(2-thenoylpropyl), Ph (di-HCl salt), 214-15.5° [4-(2-anisyl) analog (di-HCl salt) m. 213-14.5°]; γ-(4-fluorobenzoylpropyl), 2-anisyl (di-HCl salt), 212-13°; 1-(γ-(4-anisoylpropyl)-4-phenylpiperazine, m. 85-6.2°, was obtained by adding dropwise 180.9 g. 1-phenyl-4-(cyanopropyl)piperazine in 700 cc. Et<sub>2</sub>O to a stirred solution of 211 g. 4-anisylmagnesium bromide in 700 cc. Et<sub>2</sub>O, refluxing 1 hr. treating with dilute HCl, heating gently the aqueous solution 1 hr., and extracting the alkali solution with CHCl<sub>3</sub>.

IT 1535-11-1 Butyrophene, 4'-fluoro-4-(3-methyl-2-phenyl-1-piperazinyl)-, dihydrochloride (preparation of)  
BN 1535-11-1 CAPLUS  
CN Butyrophene, 4'-fluoro-4-(3-methyl-2-phenyl-1-piperazinyl)-, dihydrochloride (6Cl, 8Cl) (CA INDEX NAME)



● 2 HCl

L7 ANSWER 113 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
ACCESSION NUMBER: 1959:111827 CAPLUS  
DOCUMENT NUMBER: 53:111827  
ORIGINAL REFERENCE NO.: 53:20072d-1,20073a  
TITLE: Synthesis of 3,3-disubstituted-2-piperazines  
AUTHOR(S): Kametani, Tetsuji; Taub, Wm.; Ginsburg, David  
CORPORATE SOURCE: Israel Inst. Technol., Haifa  
SOURCE: Bulletin of the Chemical Society of Japan (1958), 31, 860-1  
CODEN: BCSJAH, ISSN: 0009-2673  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
AB cf. Hodgson, et al., C.A. 49, 5439g. Several 3,3-disubstituted-2-piperazines were synthesized for pharmacol. testing as potential hypnotics. Di-Et methyl-sec-butyl-malonate (II), b<sub>10</sub> 110° approx. 123°, was prepared in 73% yield by alkylation of di-Et methylmalonate with MeCH<sub>2</sub>Br in the presence of EtONa. α-sec-Butylpropionic acid was prepared in 66% yield by refluxing 1 hr. with 20% aqueous aq. KOH, acidifying with 10% HCl, extracting with Et<sub>2</sub>O, and decarboxylating the crude malonic acid (II) at 200°. α-Bromo-α-sec-butylpropionic bromide (III), b<sub>10</sub> 114° approx. 21°, was obtained in 86% yield by treating 6.8 g. II in the usual way with 0.68 g. red P and 6.8 ml. Br<sub>2</sub>. α-bromo-α-sec-butylpropionic acid (IV), b<sub>10</sub> 116°, was prepared in 68% yield by the usual procedure from 25.5 g. freshly distilled III and 4.4 g. EtOH. IV (15.4 g.) in 100 ml. dry EtOH was added dropwise with stirring at room temperature during 3 hrs. to 50 g. EtONa in 30 ml. dry EtOH added to the boiling solution during 30 min., refluxing continued 2 addnl. hrs., excess EtOH and H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> distilled in vacuo, Me<sub>2</sub>CO added to the residue, the precipitate filtered off, the mother liquor evaporated and Me<sub>2</sub>CO again added, and the residue distilled at 0.2 mm.

yield 3-methyl-3-sec-butyl-2-piperazinone, m. 58-61° (petr. ether); hydrobromide m. 203-4° (absolute EtOH-Et2O). An Et2O solution of III added to excess H2NCH2CH2NH2 in CHCl3 at 0° gave a precipitate. After refluxing 3 hrs., a brown insol. oil was obtained which solidified on standing. Recrystn. from C6H6 gave a product, m. 172-4°, which gave a neg. test with aqueous AgNO3. Its analysis was unsatisfactory, but it appeared to be the α,α-dibromo diimide. Methylphenylacetate (VI), m. 60°, was prepared from 25 g. Ph2CHCO2H, 500 ml. MeOH, and 25 ml. concentrated H2SO4. The mixture was refluxed 3 hrs., the MeOH removed in vacuo, the residue poured into ice water, and the oil which solidified recrystd. from aqueous EtOH. V (2.26 g.), 15 ml. CCl4, and 1.82 g. N-bromosuccinimide were refluxed 6 hrs. to give after the usual workup 2.77 g. oily Me α-bromodiphenylacetate (VI). Crude VI (2.5 g.), 1.2 g. H2NCH2CH2NH2, and 10 ml. dry CHCl3 were refluxed 4 hrs. and the mixture was kept overnight; a red oil separated which later solidified; it appeared to be a hydrobromide of H2NCH2CH2NH2. The CHCl3 solution was evaporated to dryness

and

the glassy residue triturated with C6H6 to afford 2.3 g. 3,3-diphenyl-2-piperazinone, m. 163°; picrate m. 248-9° (EtOH). α-phenylethylacetate (VII), b. 225-8°, was obtained in 91% yield by esterification of the acid as described above for V. Me α-bromo-α-phenylethylacetate (VIII) was obtained by bromination of 17.0 g. VII with 20.0 g. N-bromosuccinimide in 100 ml. CCl4 during 4 hrs. and after the usual work up gave 94% crude ester. 3-Ethyl-3-phenyl-2-piperazinone, b.p. 140° approx. 160°, was prepared as an oil in poor yield from crude VIII and H2NCH2CH2NH2 as described for the preparation of 3-methyl-3-sec-butyl-2-piperazinone. Although the desired hypnotic activity was present in several of the compds., it did not appear sufficient for further extension.

IT 22476-76-2, 2-Piperazinone, 3,3-diphenyl- 100253-41-6,  
2-Piperazinone, 3-ethyl-3-phenyl- 860229-16-9, 2-Piperazinone,  
3,3-diphenyl-, picrate  
RM 22476-76-2 CAPLUS  
CN Piperazinone, 3,3-diphenyl- (8CI, 9CI) (CA INDEX NAME)



RM 100253-41-6 CAPLUS  
CN 2-Piperazinone, 3-ethyl-3-phenyl- (6CI) (CA INDEX NAME)



RM 860229-16-9 CAPLUS  
CN 2-Piperazinone, 3,3-diphenyl-, picrate (6CI) (CA INDEX NAME)

CM 1

CRN 22476-76-2  
CMF C16 H16 N2 O

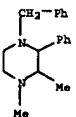
(preparation of)  
RM 101260-46-2 CAPLUS  
CN Piperazine, 1-butyl-3-methyl-2-phenyl- (6CI) (CA INDEX NAME)



RM 101784-82-1 CAPLUS  
CN Piperazine, 1-benzyl-3-methyl-2-phenyl- (6CI) (CA INDEX NAME)



RM 102008-15-1 CAPLUS  
CN Piperazine, 1-benzyl-3,4-dimethyl-2-phenyl- (6CI) (CA INDEX NAME)



RM 111440-10-9 CAPLUS  
CN Piperazine, 1-benzyl-3-methyl-2-phenyl-, hydrochloride (6CI) (CA INDEX NAME)

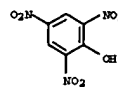


● 8CI



CM 2

CHN 88-89-1  
CMF C6 H3 N3 O7



L7 ANSWER 114 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1959-94883 CAPLUS  
DOCUMENT NUMBER: 53:94883  
ORIGINAL REFERENCE NO.: 53:17156g-i  
TITLE: Piperazine derivatives  
INVENTOR(S): Haberl, Roman  
DOCUMENT TYPE: Patent  
LANGUAGE: Unavailable  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AT 201601		19590110	AT	
AB				
New racemic or optically active piperazine deriva. are prepared by condensing racemic or optically active N-substituted 1,5-dihalo-3-azapentenes with primary amines and optionally preparing the respective salts by reaction with inorg. or organic acids, or the respective quaternization products by reaction with alkyl or benzyl halides. Preferably, condensation is effected in the presence of an addnl. alkaline condensing agent and an aqueous organic solvent between room temperature and approx. 80-120°. Thus, a solution of 2.0 g. N-(β-chloroethyl)-1-chloro-1-phenyl-2-aminopropane, 0.8 g. Et3NH2, and 1 g. dry K2CO3 in 30 cc. EtOH was refluxed 9 hrs., filtered, the filtrate evaporated in vacuo, petr. ether added to the residue, cooled, and the precipitate filtered off, to give 0.7 g. 1-benzyl-2-phenyl-3-methylpiperazine, m. about 133°, HCl salt m. 268° (decomposition). In similar manner, 1,2-diphenyl-3-methylpiperazine, b.p. 0.05 156° (HCl salt m. about 274° (decomposition)), 1-butyl-2-phenyl-3-methylpiperazine, b.p. 0.05 90-100°, 1-benzyl-2-phenyl-3,4-dimethylpiperazine, b.p. 0.01 130-40°, and 1,2-diphenyl-3,4-dimethylpiperazine, b.p. 0.01 120°, m. about 68°, have been prepared. The salts of the new compds. are of therapeutical value.				
IT				
101260-46-2, Piperazine, 1-butyl-3-methyl-2-phenyl- 101784-82-1, Piperazine, 1-benzyl-3-methyl-2-phenyl- 102008-15-1, Piperazine, 1-benzyl-3,4-dimethyl-2-phenyl- 111440-10-9, Piperazine, 1-benzyl-3-methyl-2-phenyl-, hydrochloride				

TITLE: Preparation of C-methyl-C-phenyl substituted piperazines  
AUTHOR(S): Haberl, R.  
CORPORATE SOURCE: Univ. Vienna  
SOURCE: Monatshefte fuer Chemie (1958), 89, 798-805  
CODEN: MOCMB7; ISSN: 0026-9247  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
OTHER SOURCE(S): CASREACT 58:72603  
GI For diagram(s), see printed CA issue.  
AB N-(β-Hydroxyethyl)-DL-norephedrine (I) and N-(β-hydroxyethyl)-DL-ephedrine (II) were converted to the corresponding chloro compds., ClCHPhCHMeNHCH2CH2Cl (III) and ClCHPhCHMeNHMeCH2CH2Cl (IV), and transformed by ring closure with primary aliphatic and aromatic amines to the corresponding substituted 3-methyl-3-phenylpiperazines.  
RM, CM, CHPh, R', CH2, CH2 (V). I. HCl (80.0 g.) heated 30 min. with 240 ml. SOCl2 at about 50°, the excess SOCl2 evaporated in vacuo, the residue decomposed with cracked ice and the solution made strongly alkaline, the product extracted with Et2O, the dried (Na2SO4) extract evaporated, and the residue distilled yielded 60.5% III, b.p. 1.85°, HCl salt m. 177° (decomposition) (alc.); p-nitrobenzoate m. 173° (petr. ether). I. HCl (20.0 g.) stirred at -20° (ice-salt cooling) in 200 ml. CHCl3 and gradually treated with 40 g. PCl5, the CHCl3 distilled in vacuo and the residue cautiously decomposed with water, made strongly alkaline, and extracted with Et2O yielded 53.8% III. II. HCl (30.0 g.) treated with 90 ml. SOCl2 and the mixture worked up as above yielded 60.5% IV, b.p. 110°. III (10.0 g.) and 8.0 g. PhNH2 refluxed 8 hrs. in 10 ml. absolute alc., the alc. distilled in vacuo and the residue decomposed with water, the mixture made strongly alkaline, extracted with Et2O, and the dried (Na2SO4) extract distilled yielded 60% V (R = H, R' = Ph) (VI), b.p. 0.05 156°, HCl salt m. 270-4° (decomposition). Similarly, III and IV were converted into V by treatment with the appropriate primary amine (dichloro compds., primary amine, piperazine (R, R' given), m.p. or b.p./mm., and % yield given): III, PhNH2, H, Ph, 156°/0.05, 60; III, PhCH2NH2, H, PhCH2 (VII), 133°, 12.1; III, BuNH2, H, Bu, 95°/0.05, 80; IV, PhNH2, Me, Ph (VIII), 68° (120°/0.01), 99; IV, PhCH2NH2, Me, PhCH2 (IX), 130-40°/0.01, 69; III (38.2 g.) and 19.7 g. iso-PhNH2 in 40 ml. absolute alc. refluxed 8 hrs. and the mixture worked up gave 31.0 g. Me2CHNHCHPhCHMeNHCH2CH2Cl, b.p. 0.01 65°, HCl salt m. 203°. VII (2.0 g.) in 150 ml. alc., 10 ml. N HCl, and 40 ml. H2O hydrogenated 6 hrs. with 0.2 g. 10% Pd-C, the filtered solution evaporated in vacuo, the residue taken up in a min. of water and made strongly alkaline, extracted with Et2O, and the dried (Na2SO4) extract evaporated gave 1.3 g. crystals, recrystd. with cooling from petr. ether to give V (R = R' = H), m. 78°, HCl salt m. 290-5° (sublimation). IX (3.5 g.) in 150 ml. alc., 30 ml. 0.1N HCl, and 30 ml. H2O hydrogenated 5 hrs. with 0.2 g. 10% Pd-C, the filtered solution evaporated, and the residue worked up yielded 94% V (R = Me, R' = H).  
m. 61° (after sublimation at 50°/0.001 mm.), HCl salt m. 170-84° (decomposition). VIII (1.1 g.) heated 14 hrs. on a steam bath with 1 g. HCHO and 1 g. HCO2H, the mixture treated with 1 ml. concentrated HCl and evaporated, the residue taken up in water and the solution made strongly alkaline, extracted with Et2O, and the dried (Na2SO4) extract distilled yielded 60% IX.  
IT 104096-26-6, Piperazine, 2-methyl-3-phenyl-  
RM 104096-26-6 CAPLUS  
CN Piperazine, 2-methyl-3-phenyl- (6CI, 9CI) (CA INDEX NAME)

L7 ANSWER 115 OF 120 CAPLUS COPYRIGHT 2005 ACS on STM  
ACCESSION NUMBER: 1959-94883 CAPLUS  
DOCUMENT NUMBER: 53:72603  
ORIGINAL REFERENCE NO.: 53:13169d-1, 13170a



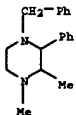
IT 101260-46-2, Piperazine, 1-butyl-3-methyl-2-phenyl-  
101784-82-1, Piperazine, 1-benzyl-3-methyl-2-phenyl-  
102008-15-1, Piperazine, 1-benzyl-3,4-dimethyl-2-phenyl-  
110489-42-4, Piperazine, 1-benzyl-3,4-dimethyl-2-phenyl-,  
hydrochloride 111440-10-9, Piperazine, 1-benzyl-3-methyl-2-  
phenyl-, hydrochloride 131254-31-4, Piperazine,  
1-butyl-3-methyl-2-phenyl-, hydrochloride 860224-68-6,  
Piperazine, 1,2-dimethyl-3-phenyl-, hydrochloride 860224-73-3,  
Piperazine, 1,2-dimethyl-3-phenyl-  
(preparation of)  
RN 101260-46-2 CAPLUS  
CN Piperazine, 1-butyl-3-methyl-2-phenyl- (6CI) (CA INDEX NAME)



RN 101784-82-1 CAPLUS  
CN Piperazine, 1-benzyl-3-methyl-2-phenyl- (6CI) (CA INDEX NAME)



RN 102008-15-1 CAPLUS  
CN Piperazine, 1-benzyl-3,4-dimethyl-2-phenyl- (6CI) (CA INDEX NAME)



RN 110489-42-4 CAPLUS  
CN Piperazine, 1-benzyl-3,4-dimethyl-2-phenyl-, hydrochloride (6CI) (CA INDEX NAME)

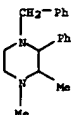


● HCl

RN 860224-73-3 CAPLUS  
CN Piperazine, 1,2-dimethyl-3-phenyl- (6CI) (CA INDEX NAME)



L7 ANSWER 116 OF 120 CAPLUS COPYRIGHT 2005 ACS ON STN  
ACCESSION NUMBER: 1956:52646 CAPLUS  
DOCUMENT NUMBER: 50:52646  
ORIGINAL REFERENCE NO.: 50:10099g-1,10100a-1,10101a-d  
TITLE: Cyclization of  $\alpha$ -( $\beta$ -aminoethylamino) ketones. Peroxides of 2,3-diphenyl-2,3-dehydropiperazines  
AUTHOR(S): Lunsford, Carl D.; Lutz, Robert E.; Bowden, Edward E.  
CORPORATE SOURCE: Univ. of Virginia, Charlottesville  
SOURCE: Journal of Organic Chemistry (1955), 20, 1513-30  
CODEN: JOCEAH; ISSN: 0022-3263  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
OTHER SOURCE(S): CASREACT 50:52646  
G1 For diagram(s), see printed CA issue.  
AB cf. C.A. 42, 7745d; 49, 9883g. To study further the effect of structure on the ring-chain tautomerism of  $\alpha$ -( $\beta$ -hydroxyethylamino) ketones an attempt has been made to prepare the  $\alpha$ -( $\beta$ -aminoethylamino)- $\alpha$ -phenylacetophenone analogs,  $\text{EtCHPhNHCHECH}_2\text{NHR}^1$  and  $\text{HOCHPh.CHPh.NR.CH}_2\text{CH}_2\text{NR}^1$ . Heating  $\alpha$ -( $\beta$ -hydroxyethylamino)- $\alpha$ -phenylacetophenone with a large excess of  $\text{SOCl}_2$  20 min. at  $70^\circ$  gives 45%  $\alpha$ -( $\beta$ -chloroethylamino)- $\alpha$ -phenylacetophenone-HCl (I), m.  $133.5^\circ$  (free base m.  $65.6^\circ$ , decompose on standing).  $\alpha$ -(N-( $\beta$ -chloroethyl)ethylamino)- $\alpha$ -phenylacetophenone (II), 57%, m.  $49.9.5^\circ$  [HCl salt has  $\lambda_{\text{maximum}}$  248 m $\mu$ ,  $\epsilon$  12,320 (EtOH)]. Refluxing 1 g. II 4 hrs. in 10 cc. EtO and 15 drops concentrated HCl, making the solution basic, and extracting with EtO give 43% 4-ethyl-2-hydroxy-1,2-diphenylmorpholine-HCl.  $\alpha$ -(N-Benzyl- $\beta$ -chloroethylamino)- $\alpha$ -phenylacetophenone (III), 70%, m.  $94.5.6^\circ$ , is relatively stable at  $20^\circ$  (HCl salt, m.  $185.6^\circ$ ). Refluxing 1 g. III 2 min. in 10 cc. absolute EtOH containing 0.07 g. Na, then adding another 10 cc. EtOH, refluxing the solution min., and filtering the hot soluble give 56% O.CPh.N(CH<sub>2</sub>Ph).CH<sub>2</sub>.CH<sub>2</sub> (IV), m.  $136.5.8.5^\circ$ . Under the same conditions O.CPh.(OH).CHPh.N(CH<sub>2</sub>Ph).CH<sub>2</sub>.CH<sub>2</sub> does not give IV. Adding (15 min.) 9.1 g. III in 500 cc. EtO to 1.5 g. LiAlH<sub>4</sub> in 200 cc. EtO, keeping the mixture



● HCl

RN 111440-10-9 CAPLUS  
CN Piperazine, 1-benzyl-3-methyl-2-phenyl-, hydrochloride (6CI) (CA INDEX NAME)



● HCl

RN 131254-31-4 CAPLUS  
CN Piperazine, 1-butyl-3-methyl-2-phenyl-, hydrochloride (6CI) (CA INDEX NAME)



● HCl

RN 860224-68-6 CAPLUS  
CN Piperazine, 1,2-dimethyl-3-phenyl-, hydrochloride (6CI) (CA INDEX NAME)

0.5 hr., adding H<sub>2</sub>O and concentrated KOH, extracting with Et<sub>2</sub>O, and treating the extract with HCl in Et<sub>2</sub>O gives 18.5% 2-(N-benzylethylamino)-1,2-diphenylethanol-HCl, m.  $228.5.9^\circ$ . Heating 4 hrs. under partial reflux 3.1 g. I, 8.2 g. (Me<sub>2</sub>CHO)3Al, and 100 cc. Me<sub>2</sub>CHOH, collecting 40 cc. distillate, evaporating the solution in vacuo, and treating the residue with 30% aqueous NaOH give 51% 2-(2-chloroethylamino)-1,2-diphenylethanol (V), m.  $138.5.9.5^\circ$  (HCl salt, m.  $218.20^\circ$ ). Adding 10 g. I in small portions to 1.5 g. LiAlH<sub>4</sub> in 100 cc. absolute Et<sub>2</sub>O, stirring the mixture another 20 min., and hydrolyzing it with 50% KOH give 85% V. Refluxing 1.5 g. V. HCl 10 min. with 5 cc. SOCl<sub>2</sub> gives 70% 2-chloro-1-( $\beta$ -chloroethylamino)-1,2-diphenylethanol-HCl, m.  $214.16^\circ$  (decomposition). Heating 6.2 g. I and 20 g. PhCH<sub>2</sub>NH<sub>2</sub> 2 hrs. at  $83^\circ$ , extracting the mixture with Et<sub>2</sub>O, and concentrating the washed (H<sub>2</sub>O) and dried extract in vacuo give 39% 1-benzyl-2,3-diphenyl-2,3-dehydropiperazine peroxide (VI), m.  $117.18^\circ$  (decomposition); with EtOH as a solvent 33% VI is obtained. From the mother liquors  $\text{BaNHCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{Ph})_2$  (VII) is isolated in considerable amount. Heating 2 g. III in 20 cc. EtOH containing 0.055 mole NH<sub>3</sub> 1-2 hrs. at  $75^\circ$  under pressure and pouring the mixture into H<sub>2</sub>O give 42% VI, which is also obtained in 43% yield when 16.5 g. PhCH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> (VIII), 21.2 g. benzoin, and 1 g. P<sub>2</sub>O<sub>5</sub> are heated 2-3 hrs. at  $100^\circ$ . VI decompose partially on standing for some time or on recrystn. from EtOH or dioxane and forms VII, m.  $186.7^\circ$ . VII is synthesized by treating VIII with BzCl in a Schotten-Baumann reaction. Heating 1 g. VI in 25 cc. 3N HCl 10 min. at  $100^\circ$ , making the cooled solution alkaline, filtering off the benzyl formed, and treating the filtrate with BzCl give almost 100% VII. Catalytic reduction of 1.78 g. VI 24 hrs. with 0.63 g. PtO<sub>2</sub> in 100 cc. 95% EtOH causes the absorption of 3 moles H with the formation of 72% 2-( $\beta$ -(benzylamino)ethylamino)-1,2-diphenylethanol (IX), m.  $106.5.7.5^\circ$ , which is also obtained in 93% yield when 7.6 g. V and 10 cc. PhCH<sub>2</sub>NH<sub>2</sub> are heated 3 hrs. at  $100^\circ$ . Adding in small portions 9.4 g. VI to 4 g. LiAlH<sub>4</sub> in 400 cc. absolute Et<sub>2</sub>O at such a rate as to maintain gentle reflux, stirring the mixture another 3 hrs., and hydrolyzing it with 40% KOH give 70% 1-benzyl-2,3-diphenylpiperazine (X), m.  $112.13^\circ$ , which is identified by conversion with PhCH<sub>2</sub>NH into 1,4-dibenzyl-2,3-diphenylpiperazine (XI), m.  $105.5.6^\circ$ . Adding slowly 2.34 g. 2,3-diphenyl-5,6-dihydropyrazine (XII) in 250 cc. Et<sub>2</sub>O to 0.5 g. LiAlH<sub>4</sub> in 100 cc. absolute Et<sub>2</sub>O with gentle reflux, stirring the mixture 4 hrs., and decomposing it with 20% KOH give 84%  $\beta$ -2,3-diphenylpiperazine which (0.6 g.), refluxed 3 hrs. with 0.06 g. PhCH<sub>2</sub>NH and 1.38 g. EtOOC in 100 cc. 95% EtOH, gives XI. (VIII), 21.2 g. III to 5.3 g. PhCH<sub>2</sub>NH<sub>2</sub> in 50 cc. absolute EtOH and refluxing the mixture 1 hr. give 83% 1,4-dibenzyl-2,3-diphenyl-2,3-dehydropiperazine (XIII), m.  $120.1^\circ$ , which is recovered unchanged when refluxed 1 hr. at  $100^\circ$  with 3N HCl. Adding (0.5 hr.) 11.5 g. desyl chloride (XIV) to 24 g. (Ph<sub>2</sub>NHCH<sub>2</sub>Ph)<sub>2</sub> (XV) in 200 cc. C<sub>6</sub>H<sub>6</sub>, refluxing the mixture 1 hr., filtering off the XV.HCl, and concentrating the filtrate give 22% XIII. When the experiment is carried out in EtOH instead of C<sub>6</sub>H<sub>6</sub>, 1,4-dibenzyl-2-ethoxy-2,3-diphenylpiperazine (XVI) is formed instead of XIII. In a typical experiment, 12 g. XV and 5.8 g. XIV are refluxed 2 hrs. in EtOH and the mixture is kept overnight, giving 23% XIII, pouring the alc. mother liquor into H<sub>2</sub>O gives 3% XVI, m.  $94.6^\circ$ . In 1 experiment 40% XVI was obtained. Refluxing XVI 3 hrs. with LiAlH<sub>4</sub> in Et<sub>2</sub>O is without effect. An attempt to prepare the 2-methoxy analog led only to XIII. Adding (45 min.) 11.5 g. XIV to 30 g. (CH<sub>2</sub>NH<sub>2</sub>)<sub>2</sub> at  $70^\circ$ , pouring the mixture into H<sub>2</sub>O, and making the solution alkaline with Na<sub>2</sub>CO<sub>3</sub> give 41% XII, m.  $157.60^\circ$ . Heating 21.2 g. benzoin, 17.5 g. Et<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, and 1 g. P<sub>2</sub>O<sub>5</sub> 4 hrs. on a water bath, extracting with Et<sub>2</sub>O, and treating the washed and dried Et<sub>2</sub>O solution with HCl-Et<sub>2</sub>O give 33%  $\alpha$ -( $\beta$ -diethylaminoethylamino)- $\alpha$ -phenylacetophenone-2HCl.H<sub>2</sub>O, m.  $231.4^\circ$  (decomposition), which (5 g.), reduced with 0.91 g. LiAlH<sub>4</sub> in Et<sub>2</sub>O, gives 75% 2-( $\beta$ -diethylaminoethylamino)-1,2-diphenylethanol, m.  $103.5.5.5^\circ$ .

Condensation of I with EtOH gives 34% 2,3-diphenyl-1-ethyl-2,3-dehydropiperazine peroxide (XVII), m. 103-3.5°, when the reaction is carried out 1 hr. at 65°. 43% XVII is obtained and, in the presence of P2O5, the yield is 53%. XVII liberates iodine from acidified KI. Heating 1 g. H<sub>2</sub>NCHPhCH<sub>2</sub>NH<sub>2</sub>, 1.5 g. benzoin, and 0.02 g. P2O5 2 hrs. on a steam bath, dissolving the resulting sirup in 6 cc. 95% EtOH, and adding 2 cc. concentrated HCl gives 76% α-(β-aminoethylamino)-α-phenylacetophenone-2HCl (XVIII), m. 224° (decomposition). XVIII, kept in H2O, is hydrolyzed to 1,2,3-triphenyl-2,3-dehydropiperazine (XIX), m. 117°, which was formulated by Gabriel and Eschenbach (Ber. 31, 1501 (1898)) as 1,2,3-triphenyl-3,4-dehydropiperazine. When XIX is treated with concentrated HCl 1 hr. XVIII crystallizes. Passing dry air 1 hr. into 1 g. XIX in Et2O with ice-cooling gives 64% XIX peroxide, m. 126° (decomposition). Adding slowly 1 g. XVIII to 0.5 g. LiAlH4 in 200 cc. Et2O, stirring the mixture 1 hr., and hydrolyzing it with concentrated KOH gives 96% 2-(β-aminoethylamino)-1,2-diphenylethanol (XX), m. 133-5.5°. When 2.75 g. V and 2 g. PhNH2 are refluxed 2 hrs. in 20 cc. 95% EtOH, 68% XX.HCl, m. 226.5-7° (decomposition), is obtained. Refluxing 2 g. PhNH2, 3.1 g. I, and 10 cc. 95% EtOH 12 hr., partitioning the reaction mixture between Et2O and EtOH, and recrystg. the residue of the Et2O solution give 55% α-amino-β-phenylacetophenone, m. 96.5-8°, which is also obtained in 16% yield when XVII and PhNH2 are refluxed 6.5 hrs. in EtOH. The factors influencing the ring-chain tautomerism of α-(β-aminoethylamino) ketones are discussed. Cyclization is favored by the tertiary character of the α-N and by the basic and secondary character of β-N. 31 references.

IT 143699-24-5, Piperazine, 2,3-diphenyl- 146362-57-4, Piperazine, 1-benzyl-2,3-diphenyl- (preparation of)

RN 143699-24-5 CAPLUS

CN Piperazine, 2,3-diphenyl- (9CI) (CA INDEX NAME)



RN 146362-57-4 CAPLUS

CN Piperazine, 2,3-diphenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L7 ANSWER 117 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1949:21375 CAPLUS

DOCUMENT NUMBER: 42:21375

ORIGINAL REFERENCE NO.: 42:4581h-1,4582a-e

TITLE: Experimental chemotherapy of filariasis. IV. The preparation of derivatives of piperazines

AUTHOR(S): Stewart, H. W.; Turner, R. J.; Denton, J. J.; Kushner, S.; Brancove, L. M.; McEwen, W. L.; Hewitt, R. I.; Sbarrow, Y.

CORPORATE SOURCE: Am. Cyanamid Co., Pearl River, NY



RN 856842-25-6 CAPLUS

CN Piperazine, 2,3-diphenyl-, dihydrochloride (5CI) (CA INDEX NAME)



●2 HCl

L7 ANSWER 118 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1947:25293 CAPLUS

DOCUMENT NUMBER: 41:29293

ORIGINAL REFERENCE NO.: 41:5886e-g

TITLE: The configuration of geometrical isomers of 2,3-diphenylpiperazine

AUTHOR(S): Hayashi, Taro

SOURCE: Scientific Papers of the Institute of Physical and Chemical Research (Japan) (1941), 38, 466-86

CODEN: SPIPAQ; ISSN: 0020-3092

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB The constitution of α- and β-2,3-diphenylpiperazines, which were obtained by the reduction of 2,3-diphenylpyrazine, was confirmed by the preparation from 5,6-diphenyl-2,3-dihydropyrazine and 2,3-diphenyl-2,3-dihydropyrazine. The multiplicity of the piperazine ring is discussed. The resolvability of α- and β-diphenylpiperazines was tested by the recrystn. of the meso-d-tartrate and α-bromocamphor-α-sulfonate of the α-isomer and the α-bromocamphor-α-sulfonate and d-methylcamphor derivative of the β-isomer. After fractional recrystn., α-diphenylpiperazine showed a small rotatory power, but the β-isomer showed no rotatory power. It is concluded that the α-isomer has the trans form and the β-isomer the cis form. The absorption spectra of the α- and β-isomers are quite similar.

IT 143699-24-5, Piperazine, 2,3-diphenyl- (preparation of)

RN 143699-24-5 CAPLUS

CN Piperazine, 2,3-diphenyl- (9CI) (CA INDEX NAME)



SOURCE: Journal of Organic Chemistry (1948), 13, 134-43

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 42:21375

AB For diagram(s), see printed CA issue.

G1 cf. C.A. 42, 2019b. Some mono- and di- substituted piperazine deriva. EtOH, CH2Cl2, CH2Cl2 (I) are prepared to be tested as antifilarials. Hydrolysis of the 1-carbethoxy-4-alkylpiperazines with concentrated HCl according to Moore, et al. (C.A. 23, 2183), gives the corresponding 4-alkylpiperazines. The following I are prepared (R and R' given): Me, H (II), 74% yield, b760 134-6° (di-HCl salt, 96.6%, crystallizing with 1 H2O, m. 82.5-3° (corrected)); Me, Me, 70%, b760 131-3° (corrected) (di-HCl salt, crystallizing with 2/3 H2O, m. 251.5-3° (corrected) (decomposition)); Me, CH2CH2CH2CH2, di-HCl salt, 58%, m. 262-4°, MeOH, H, di-HCl salt (III), 90%, m. 274-5° (decomposition), Ph, H (IV), 31.5%, b15 161-4° (corrected) (di-HCl salt m. 245-7° (corrected)); Ph, Me, 70.5%, b6 130-1° (corrected) (di-HCl salt, 94.5%, m. 180-2° (corrected) (decomposition)); MeO2C, H, 37%, b7 112-16°; MeO2C, Me, 16%, m. 116-21°; MeO2C, MeO2C, 24, b11 163°, EtO2C, H (V), di-HCl salt, 47%, m. 156.5-7° (corrected); EtO2C, Me (VI), 94%, b6 97-8° (corrected) (di-HCl salt, 94%, m. 169-9° (corrected)); EtO2C, Et (VII), 82%, b28 132°, EtO2C, Pr (VIII), 73%, b16 136° (di-HCl salt m. 189-92°); EtO2C, iso-Pr (IX), 75%, b19 138-44°; EtO2C, Bu (X), 64%, b8 139-40°; EtO2C, iso-Bu, 63%, b1 93.5-4°; EtO2C, sec-Bu (XI), 40%, b18 139-47° (di-HCl salt m. 218-21° (decomposition)); EtO2C, n-C7H15, 66%, b4 159-61° (corrected); EtO2C, MeCH2CH2, 81.7%, b5 113-15° (corrected); EtO2C, HOCH2CH2, 72%, b12 175-7°; EtO2C, EtO2CCH2, 75%, b2 123-5°; EtO2C, Ph, prepared in 92% yield by refluxing 54.7 g. IV, 2HCl, 29.8 g. EtO2COCl, and 69.2 g. NaHCO3 in 150 cc. absolute EtOH 3 hrs., m. 61-1.5° (corrected) (di-HCl salt m. 197-8° (corrected) (decomposition)); EtO2C, PhCH2, di-HCl salt, 86%, m. 218-18.5° (corrected); EtO2C, EtCO, 87%, b3 131-3°, m. 45-6°, BuO2C, H, 46%, b10 141-3°; BuO2C, BuO2C, 5.2%, b10 205-8°; iso-BuO2C, H, 52%, b13 138-42°; iso-BuO2C, iso-BuO2C, 7.3%, b15 203-5°. Bis(1-carbethoxy-4-piperazinyl)methane, 95.7%, m. 61.5-2.5° (corrected); 1,2-bis-(1-carbethoxy-4-piperazinyl)ethane, 86.4%, b12 258-62° (corrected), m. 80-80.5°.

2,3-Diphenyl-5,6-dihydropyrazine (150 g.) hydrogenated in 350 cc. absolute EtOH in the presence of CuO-Cr2O3 2 hrs. at 150° and 1000 lbs., gives 72.5% β-2,3-diphenylpiperazine (XII), m. 108-9° (corrected) (di-HCl salt (XIIa) m. 310-11° (corrected) (decomposition)); XII regenerated from XIIa m. 110-10.5° (corrected). SO2Cl2 (4 g.) added to 10 g. II in 30 cc. ice-cooled CHCl3 gives 32% 1,1'-sulfonylbis(4-methylpiperazine), m. 89-90.5°. Refluxing 10 g. Et2NCH2CH2N.HCl, 13.4 g. II, 2HCl.H2O, and 14.9 g. Na2CO3 in 100 cc. 95% EtOH 18 hrs. gives 1-methyl-4-(2-dimethylaminomethyl)piperazine-2HCl, m. 262-4°.

1-Carbethoxy-2(37)-methylpiperazine, 60%, b10 127-9°; 1,4-dicarbethoxy-2-methylpiperazine (XIII), 74%, b16 173-5°. Of these compds. II, III, VI-X, and XIII show slight, and V good antifilarial activity.

IT 143699-24-5, Piperazine, 2,3-diphenyl- 856842-25-6, Piperazine, 2,3-diphenyl-, dihydrochloride (preparation of)

RN 143699-24-5 CAPLUS

CN Piperazine, 2,3-diphenyl- (9CI) (CA INDEX NAME)

L7 ANSWER 119 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1947:25287 CAPLUS

DOCUMENT NUMBER: 41:20687

ORIGINAL REFERENCE NO.: 41:4156c-f

TITLE: Derivatives of piperazine. XXI. Synthesis of piperazine and C-substituted piperazines

AUTHOR(S): Kitchen, Leland J.; Pollard, C. B.

CORPORATE SOURCE: Univ. of Florida, Gainesville

SOURCE: Journal of the American Chemical Society (1947), 69, 854-5

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 41:20687

AB cf. C.A. 37, 5972.6. HO(CH2)2NH(CH2)2NH2 (I) (150 g.) and 5 g. Raney Ni, refluxed 2.5 hrs., give 32% piperazine (II). I (85 g.) and 10 g. Raney Ni in 400 cc. dioxane, heated 3 hrs. in an autoclave at 200°, give 51% II; Cu chromite (3 hrs. at 275°) gives 45%; CuO (3 hrs. at 275°) gives 43%; Fe (H reduced) (3 hrs. at 300°) gives 26%; activated Al2O3 (3 hrs. at 300°) gives 20%; and SiO2 gel (3 hrs. at 300°) gives 17.4%. Other catalysts give much lower yields. MeCH(OH)CH2NH(CH2)2NH2 (225 g.) and 10 g. Raney Ni in 250 ml. dioxane, heated 5 hrs. at 185-203°/200 lb./sq. in. H pressure, give 70% of the 2-Me derivative of II. PhCH(OH)CH2NH(CH2)2NH2 (108 g.) in 300 ml. dioxane, agitated with Raney Ni 3.5 hrs. at 220°, yields 32% 2-phenylpiperazine, b10 138° (m. 87.5-7.8° (m. ps. corrected); di-HCl salt m. about 335° (decomposition); di-NO derivative m. 69.9-70.2°; di-Ac derivative m. 70.1-1.2°; picrate m. about 276° (decomposition).

IT 5271-26-1, Piperazine, 2-phenyl- (and derive.)

RN 5271-26-1 CAPLUS

CN Piperazine, 2-phenyl- (7CI, 9CI, 9CI) (CA INDEX NAME)



L7 ANSWER 120 OF 120 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1946:25761 CAPLUS

DOCUMENT NUMBER: 40:25761

ORIGINAL REFERENCE NO.: 40:5074c-e

TITLE: Piperazine and derivatives

INVENTOR(S): Pollard, Cash B.; Kitchen, Leland J.

PATENT ASSIGNER(S): Board of Commissioners of State Institutions

Tallahassee

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 240022		19460507	US	

AB A method is described for the removal of H2O from N-(2-hydroxyethyl)ethylenediamine (I) and its derive. to form piperazine (II) and substituted piperazines. A mixture of 85 parts I, 400 parts dioxane (III), and 10 parts Raney Ni is heated and agitated in a closed vessel at 200 ± 5° for 3 hrs. The catalyst is removed by filtration and the filtrate distilled to give 42% (based on I used) of II, b.

140-50°. Other catalysts useful in producing II are Pd on activated charcoal, activated Al<sub>2</sub>O<sub>3</sub>, silica gel, and Cu chromite (IV). Raney Ni catalyst is also used in the absence of III as a solvent or with diethyl carbitol solvent. N-(2-Hydroxypropyl)ethylenediamine (59 parts) mixed with 350 parts III and 10 parts IV is heated under 500 lb. pressure and agitated at 275° for 3 hrs. Distillation gives 50% of 2-ethylpiperazine, b. 152.8°. 2-Phenylpiperazine, b. 138°, is prepared similarly in 33% yield from N-(2-hydroxy-2-phenylethyl)ethylenediamine.

IT 5271-26-1, Piperazine, 2-phenyl-  
(preparation of)

RM 5271-26-1 CAPLUS

CH Piperazine, 2-phenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



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